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ON THE MOLECULAR REARRANGEMENT OF *o*-AMINOPHENYLETHYL CARBONATE TO *o*-OXYPHENYLURETHANE.[1]

BY JAMES H. RANSOM.

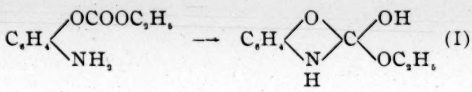
On reducing *o*-nitrophenylethyl carbonate,

$$O_2NC_6H_4OCOOC_2H_5,$$

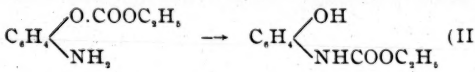
with tin and hydrochloric acid in alcoholic solution, according to Bender,[2] a white crystalline compound (melting-point 95°, as given by Bender) separates out of the acid solution. Analysis gave figures agreeing with the composition of the expected reduction-product, aminophenylethyl carbonate, $H_2NC_6H_4OCOOC_2H_5$, and this constitution has been ascribed to the compound in spite of the striking absence of basic properties. The seeming contradiction between properties and constitution led Professor Stieglitz, who recently had occasion to use the substance in connection with an investigation with Dr. H. N. McCoy,[3] to suspect that after the reduction of the nitro compound to an amine base, a molecular rearrangement of the latter produces Bender's body. Such a

[1] See a preliminary report: Ber. d. chem. Ges., **31**, 1055.
[2] Ber. d. chem. Ges., **19**, 2268.
[3] This JOURNAL, **21**, 111.

molecular rearrangement could occur in one of the following ways:



(I)

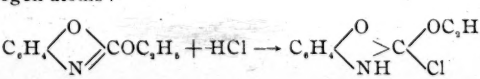
or 

(II)

The well-known ease with which *o*-aminophenols give ring compounds suggested constitution (I). The possibility of isolating and identifying a substance of such a constitution seemed particularly important and worthy of close investigation for two reasons. In the first place, in the action of amines on acid esters, and *vice versa*, of alcohols on acid amides, an intermediate addition-product is quite generally assumed to be formed according to

$$RCOOR+H_2NR \rightleftarrows RC(NHR)(OH)OR \rightleftarrows RCONHR+HOR,$$

but the addition-product has not been isolated. Formula (I) represents such an addition-product of an amine to an ester, made stable, possibly, by the general tendency towards the formation of ortho rings. In the second place formula (I) represents the constitution of the hydroxide base corresponding to the hydrochloride of ethoxymethenylaminophenol (an imido ether) if the salts of imido ethers are formed by the addition of the acid to the double bond between the carbon and nitrogen atoms:[1]



A substance of constitution (I) would have to show the most intimate relationship to this hydrochloride; and the existence or non-existence of such a relationship would go a great way towards settling the constitution of the hydrochlorides of imido ethers.

Constitution (II) would result from the migration of an acyl group from a negative phenol radical to the basic amido

[1] *Vide* Stieglitz: This JOURNAL, **31**, 101.

group. Similar migrations have been observed, occasionally, before. Notably *o*-nitrophenyl benzoate, closely related to the nitro body under investigation, gives on reduction in hot alcoholic solution benzoyl-*o*-aminophenol. Böttcher[1] showed that the anhydro base, benzenylaminophenol, is formed by loss of water in the experiment, and under the same conditions goes over into benzoylaminophenol by the addition of water:

$$NO_2C_6H_4OCOC_6H_5 \longrightarrow N{=}C_6H_4O{-}CC_6H_5 \longrightarrow C_6H_5CONHC_6H_4OH.$$

He concluded, therefore, that benzenylaminophenol is an intermediate product in the rearrangement. But a substance of formula (II) could result, without the formation of an anhydro base, by further transformation of (I), according to

$$\begin{matrix} HO \\ C_2H_5O \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} O \\ NH \end{matrix}\!\!>C_6H_4 \longrightarrow C_2H_5OCONHC_6H_4OH,$$

a change entirely analogous to the conversion of an acid ester into an acid amide, as shown on page 10.

Such a rearrangement of an aminophenyl carbonate into an oxyphenylurethane (II), demonstrated to occur only in the ortho series, and to take place without the intermediate formation of an anhydro base, would prove the intermediate formation of compound (I), and thus incidentally strongly support the modern conception of ester and amide transformations. In such an event, also, the substance of constitution (I) would be shown to have an existence, however, transitory, and it might be possible to establish, even then, some connection between it and the hydrochloride of ethoxymethenylaminophenol, although the inability to isolate the hydroxide itself would, no doubt, render such a work not only more difficult but also far less decisive in determining the constitution of the hydrochlorides of the imido ethers.

With these objects in view, the present investigation was suggested by, and carried out under the direction of, Professor Stieglitz, to determine first, the true constitution of the reduc-

[1] Ber. d. chem. Ges., **16**, 630.

tion-product of *o*-nitrophenylethyl carbonate (Bender's compound), that no opportunity might pass for isolating and investigating a possible hydroxide of constitution (I), and secondly, to study more closely than has been done by Böttcher and others the mechanism of the rearrangement after reduction.

The facts bearing on the question of the constitution of Bender's compound (m. p. 95°) known at the outset of this investigation were as follows: It crystallized out of strong acid solution and could not possibly have the constitution $H_2NC_6H_4OCOOC_2H_5$, which he assigned to it. Such a substance would have approximately the basicity of aniline and would dissolve readily in dilute hydrochloric acid (as has since been confirmed by isolating aminophenylethyl carbonate).

On the other hand, Bender prepared an acetyl derivative of his compound that on distilling gave acetylcarbonylaminophenol[1], $CH_3CO—\underset{\llcorner\!\!\lrcorner}{N}—C_6H_4—O—C=O$, which evidently is in better accord with Bender's view of the constitution, $CH_3CONHC_6H_4OCOOC_2H_5$, than, for instance, with the isomeric constitution, $CH_3COOC_6H_4NHCOOC_2H_5$. Finally Groenvik[2] had already prepared an oxyphenylurethane (II), $HOC_6H_4NHCOOC_2H_5$ (soluble in alkalies, insoluble in dilute acids), from *o*-aminophenol and ethyl chlorformate, and found its melting-point to be 85°, which is 10° lower than that of Bender's compound. On comparing the two substances I found them to be identical. After one or more recrystallizations, of preparations made a number of times, the melting-point of both bodies was found to be 86°,[3] and this was not changed by mixing the two compounds even without recrystallizing. Both dissolve easily in alkalies and give in alkaline solution the same benzoate. In view of the solubility of the substance in alkali no doubt can remain that Bender's compound was not an aminophenylethyl carbonate but had suffered molecular rearrangement to (I) or (II).

[1] Bender: Ber. d. chem. Ges., **19**, 2270.

[2] Bull. Soc. Chim., **25**, 177.

[3] The melting-point given by Bender is probably due to a typographical error or to an unreliable thermometer: *Vide*, Ber. d. chem. Ges., **19**, 2951.

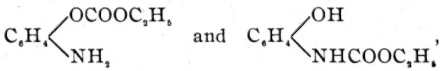
On reducing *o*-nitrophenylethyl carbonate, *o*-aminophenylethyl carbonate is undoubtedly first formed. The acid solution remains clear for some time, and the precipitation of Bender's compound is completed, in the cold, only after a day or two. By keeping the solution very cold while reducing and then rendering immediately alkaline, and extracting with ether, I was able to isolate *o*-aminophenylethyl carbonate—an oil soluble in dilute acids but insoluble in alkali—as the product of the first stage of the reaction. In the acid solution, therefore, a rearrangement of aminophenylethyl carbonate to oxyphenylurethane must occur according to

$$H_2NC_6H_4O(COOC_2H_5) \longrightarrow (COOC_2H_5)NHC_6H_4OH \text{ (II)},$$

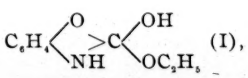
if Groenvik's oxyphenylurethane really has the constitution one would be inclined to assign to it on the basis of its solubility in alkalies and of its preparation from *o*-aminophenol and ethyl chlorformate:

$$NH_2C_6H_4OH + ClCO_2C_2H_5 \longrightarrow (CO_2C_2H_5)NHC_6H_4OH.$$

It is obvious, however, that the attempt to prepare two compounds,



could also lead to one and the same body, if in both cases the well-known tendency of the ortho series to form ring compounds was exhibited—both substances could yield the ring compound,



as the stable form. It still remained, therefore, to determine whether *o*-oxyphenylurethane has the constitution (I) or (II).

The attempt to decide this question by alkylating with methyl iodide in alkaline solution was quite unsuccessful. Most of the substance was recovered unchanged. The substance also proved to be too sensitive to the oxidizing effects of silver oxide to prepare a silver salt for the purpose of methylation (blackening occurred under all conditions).

On the other hand, acyl derivatives were so easily made in the cold, by Baumann's method, with quantitative yields, that this method of investigation was pursued next. It led to most surprising results, the experimental data of which were carefully confirmed by me by two independent investigations with an interval of half a year. By benzoylating oxyphenylurethane, as Bender's and Groenvik's compound may be called, a benzoyl derivative is obtained melting at 75°.5. If oxyphenylurethane has the constitution its name expresses (II), the benzoate should be $C_6H_5COOC_6H_4NHCOOC_2H_5$. But exactly the same benzoyloxyphenylurethane (m. p. 75°.5) was obtained by me on treating benzoyl-*o*-aminophenol,

$$HOC_6H_4NHCOC_6H_5,$$

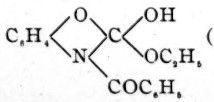
(from *o*-aminophenol and benzoyl chloride; soluble in alkalies, insoluble in acids), in alkaline solution with ethyl chlorformate. Both bodies melt at 75°.5 and there is no depression of the melting-point on mixing them. The two reactions,

$$HOC_6H_4NH\overset{*}{C}OOC_2H_5 + Cl\overset{**}{C}OC_6H_5$$

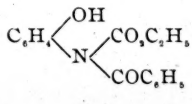
and

$$HOC_6H_4NH\overset{**}{C}OC_6H_5 + Cl\overset{*}{C}OOC_2H_5,$$

give the same product. The inevitable conclusion (excluding molecular rearrangements) is that both acyl carbon atoms, $\overset{*}{C}$ and $\overset{**}{C}$, must be attached to the nitrogen atom in benzoyloxyphenylurethane. The latter would then be


(I′)

or


(II′).

The behavior of benzoyloxyphenylurethane towards heat would seem to show that, when oxyphenylurethane is benzoylated, the benzoyl group goes to the nitrogen atom. On heating it gives alcohol and benzoylcarbonylaminophenol,[1] in which the benzoyl group is found attached to nitrogen. The same substance was obtained by benzoylating carbonylaminophenol:

[1] Bender's acetaminophenylethyl carbonate shows similar behavior.

$$HNC_6H_4O{-}CO + ClCOC_6H_5 \longrightarrow C_6H_5CON.C_6H_4.O{-}CO + HCl.$$

Benzoyloxyphenylurethane is insoluble in alkalies and shows none of the properties of a phenol. An acyl group entering the urethane molecule according to

$$HOC_6H_4NHCO_2C_2H_5 + ClCOC_6H_5 \longrightarrow HOC_6H_4N(COC_6H_5)CO_2C_2H_5 + HCl,$$

would be without a parallel under the conditions observed. Phenylurethane, *o*-methoxyphenylurethane, etc., are not benzoylated under the same conditions. Consequently formula (II′) can be considered as completely disposed of as a possible constitution for benzoyloxyphenylurethane. If both acyl carbon atoms $\overset{*}{C}$ and $\overset{**}{C}$ are attached to nitrogen only formula (I′) would be left to represent the true constitution of benzoyloxyphenylurethane, and oxyphenylurethane itself would have the ring constitution

$$HNC_6H_4O{-}C(OH)OC_2H_5 \quad (I).$$

Imide groups in similar ring complexes have frequently been found to give to compounds acid properties. For instance, ethenyl-*o*-phenylenediamine,[1]

$$H.NC_6H_4N{=}C.CH_3,$$

and ethoxymethenyl-*o*-phenylenediamine,[2]

$$H.NC_6H_4N{=}COC_2H_5,$$

are soluble in alkalies, and this is undoubtedly due to the presence of the imide group (NH) in these substances. The solubility, in alkalies, of oxyphenylurethane as a ring derivative could then very well be due to the imide group, and, on benzoylating such a compound, the union of the benzoyl group with the nitrogen atom, as found above, would be expected in a normal case. The behavior of oxyphenylureth-

[1] Bamberger: Ann. Chem. (Liebig), **273**, 274.
[2] Sandmeyer: Ber. d. chem. Ges., **19**, 2654.

ane towards acyl chlorides—exactly the same results were obtained on using *m*-nitrobenzoyl chloride in place of benzoyl chloride—agrees in every detail far better, therefore, with constitution (I), $HNC_6H_4OC(OH)OC_2H_5$, than with constitution (II), $HOC_6H_4NHCO_2C_2H_5$.[1]

But in view of the fact that we were dealing with derivatives, for which one molecular rearrangement of the mother substance had already been positively proved, these conclusions were further tested as follows: Benzoyloxyphenylurethane, as $(C_6H_5CO)N.C_6H_4OC(OH)OC_2H_5$, being insoluble in alkalies, the alcoholic hydroxyl group could have no marked acid properties. Now oxyphenylmethylurethane can be prepared from methylaminophenol and ethyl chlorformate according to the equation:

$$CH_3NHC_6H_4OH + ClCO_2C_2H_5 \longrightarrow C_2H_5O_2CN(CH_3)C_6H_4OH + HCl,$$

and being in every way analogous to oxyphenylurethane, it must have an analogous constitution, and would be, as a ring derivative, $CH_3NC_6H_4OC(OH)OC_2H_5$. Such a compound, as explained in the case of benzoyloxyphenylurethane, having no acid imide group, should have no marked acid properties. On preparing oxyphenylmethylurethane it was found to dissolve quite readily in alkalies like an ordinary phenol. This result made the ring constitution for it, and consequently for oxyphenylurethane itself, again very doubtful, since the surprising nature of the acyl derivatives—verified experimentally in every point again—could very well be due to molecular rearrangements (see below) analogous to the proved rearrangement of aminophenylethyl carbonate. Recourse was had, therefore, in the final instance to methylation of oxyphenylurethane with diazomethane in neutral solution, following Von Pechmann's method for determining delicate questions of constitution. Von Pechmann[2] has shown that substances of an acid or a phenol character are easily methylated with this

[1] See preliminary report, *loc. cit.*, p. 1059.

[2] Ber. d. chem. Ges., **28**, 855.

reagent in absolute ether solution, thus minimizing the probability of molecular rearrangements. Oxyphenylurethane gave with diazomethane, methoxyphenylurethane,

$$CH_3OC_6H_4NHCO_2C_2H_5,$$

recognized by converting it into methoxyphenylurea,

$$CH_3OC_6H_4NHCONH_2,$$

which was in every particular identical with a preparation made synthetically from *o*-anisidine or from *o*-anisidineurethane. The constitution of *o*-oxyphenylurethane is consequently

$$HOC_6H_4NHCO_2C_2H_5 \text{ (II)},$$

and not

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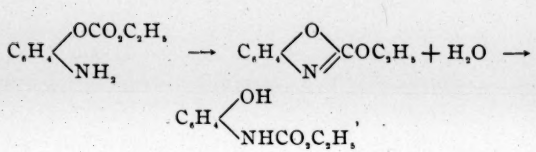


since the anhydro base is quite a stable body, having been preserved for months without excluding traces of moisture, and even in contact with water no such rapid change was observed as in the case of aminophenyl carbonate. This conclusion is confirmed by the fact that diacylaminophenols, $Ac.NHC_6H_4OAc'$, as shown below, apparently suffer similar rearrangement, even more readily than aminophenylethyl carbonate itself, and, in their case, an anhydro base as intermediate product is plainly impossible. Aminophenylethyl carbonate, therefore, suffers rearrangement without the intermediate formation of an anhydro base, as Böttcher was led to assume in the analogous case of the reduction of *o*-nitrophenyl benzoate. Nevertheless, an intermediate ring derivative is most likely formed for the following reasons:

1. *p*-Aminophenyl carbonate was found to be a perfectly stable compound, not liable to rearrangement—the rearrangement is peculiar to the ortho series.

2. The rearrangement occurs as long as the nitrogen atom holds at least one hydrogen atom, and no longer.

Thus the fact that the two reactions,

$$HOC_6H_4NHCO_2C_2H_5 + ClCOC_6H_5,$$

and

$$HOC_6H_4NHCOC_6H_5 + ClCO_2C_2H_5.$$

give one and the same substance, $C_6H_5COOC_6H_4NHCO_2C_2H_5$, (see below) is most likely due to similar rearrangements of the diacylaminophenols. But the analogous derivatives of methylaminophenol give two series of isomers; *e. g.*,

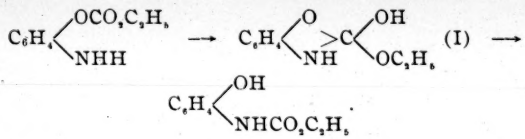
$$C_6H_5COOC_6H_4N(CH_3)CO_2C_2H_5,$$

and

$$(C_2H_5O_2C)OC_6H_4N(CH_3)COC_6H_5,$$

both of which have been prepared, which are perfectly stable substances. There is, therefore, no direct exchange of acyls in the kind of rearrangement under discussion: its de-

pendence on the hydrogen of the imide group points clearly to intermediate ring formations, which may be illustrated most simply in the rearrangement of aminophenylethyl carbonate itself:



It is obvious that at least one, but only one, reactive hydrogen atom of the amine group is essential to such rearrangements, and that the second one may be replaced by a second acyl group without interfering with the possibility of such ring transformations.

Thus, while oxyphenylurethane has not the ring constitution (I), there is every reason for believing that this ring compound has a transitory existence when aminophenylethyl carbonate goes over into oxyphenylurethane. No other rational explanation of the change seems possible on the basis of the experimental evidence presented. It follows then that derivatives, $RC(OH)NH(OR)$, of the ortho acids are formed, but have no stable existence even under the favorable conditions caused by a ring formation.

The unusual results obtained in preparing diacylaminophenols, to which frequent reference has been made, require a few words of explanation. The same benzoyloxyphenylurethane (m. p. 75°.5, always giving by saponification with alkalies benzoic acid and oxyphenylurethane), was obtained by the following three reactions:

a. The action of benzoyl chloride on oxyphenylurethane,

$$HOC_6H_4NHCO_2C_2H_5 + ClCOC_6H_5.$$

b. The action of ethyl chlorformate on benzoylaminophenol in alkaline solution,

$$HOC_6H_4NHCOC_6H_5 + ClCO_2C_2H_5.$$

c. The action of benzoyl chloride on aminophenylethyl carbonate in aqueous alkaline, or in ether, solution,

$$(CO_2C_2H_5)OC_6H_4NH_2 + ClCOC_6H_5.$$

According to its behavior on saponification, and according to preparation *a* benzoyloxyphenylurethane seems to have the constitution $C_6H_5COOC_6H_4NHCO_2C_2H_5$ (A). According to preparations *b* and *c* and their behavior when heated (p. 6) benzoyloxyphenylurethane would be

$(COOC_2H_5)OC_6H_4NHCOC_6H_5$ (B). Since the same body is produced only one of these formulæ can be the correct one. When an attempt is made to prepare the second compound it is evidently converted by rearrangement into the stable modification. Formula (A) probably represents the true constitution of the stable substance, for the reason that when saponified it yields benzoic acid and oxyphenylurethane. This method gave perfectly reliable results in determining the position of the acyl groups in the case of bodies of undoubted constitution in the methylaminophenol series,

$$AcN(CH_3)C_6H_4OAc',$$

where both series of isomers have been prepared and found to be stable. With these compounds, the acyl group attached to oxygen is, without exception, removed first by saponification with alkalies. When the compound (B) is formed by methods *b* and *c* it at once goes over into the form (A) as follows:

$$(CO_2C_2H_5)OC_6H_4\overset{*}{N}HCOC_6H_5 \longrightarrow C_6H_5COOC_6H_4NHCO_2C_2H_5.$$

As the hydrogen atom $\overset{*}{H}$ is essential for the rearrangement (when it is replaced by methyl there is no rearrangement), intermediate ring derivatives must be formed first similar to that given on page 2 as representing the rearrangement of aminophenylethyl carbonate. It is even possible that in the case of the diacyl compounds such a ring derivative represents the final form of the stable modification; for example, benzoyloxyphenylurethane may be

$$C_6H_5CONC_6H_4OC(OH)OC_2H_5,$$

which would agree, in part, somewhat better with its behavior than the constitution (A) assigned to it.

It is noteworthy that it has been possible to isolate the two isomers, aminophenylethyl carbonate and *o*-oxyphenylurethane, and to observe the change of the former into the latter, but that contrary to expectation all endeavors to isolate the corresponding second isomeric benzoyl derivative (and the second nitrobenzoyl isomer) have thus far been unsuccessful. In fact the two isomers in the series of *o*-diacylaminophenols, $AcOC_6H_4NHAc'$ and $Ac'OC_6H_4NHAc$, have in no instance been obtained with absolute certainty as yet. In the case of Ac being made benzoyl (C_6H_5CO), and Ac' *m*-nitrobenzoyl ($NO_2C_6H_4CO$) substances were obtained, crystallizing persistently in different forms, but of practically the same melting-point, (152° and 153°) which was not depressed more than 4° (softening slightly at 146°, melting at 149°–153°) on mixing the two substances. The one crystal form was twice observed to change over into the other and remain so permanently,[1] and both compounds gave the same saponification products. It is somewhat uncertain, therefore, whether they really represent chemical isomers of the two series just mentioned, but it is probable that they do. Further investigation of the constitution of the stable compounds obtained will be carried out, and further attempts made to isolate isomers in this series and observe the conditions of their change to the stable forms.

The work involved in attaining the first two objects of this investigation—determining the constitution of oxyphenylurethane and studying the rearrangements in this group—left but little time for taking up the third object, a study of the connection between the ring derivative,

$$\underset{\llcorner\!\!\!

tion at present. It was shown that the above hydrochloride gives, by hydrolysis, oxyphenylurethane under the same conditions that aminophenylethyl carbonate does. The reactions are exactly in accord with what was to be expected from hydrolysis[1] of the hydrochloride of an imido ether formed by the addition of hydrochloric acid to the double bond of ethoxymethenylaminophenol:[2]

I. $OC_6H_4N{=}COC_2H_5 + HCl \longrightarrow OC_6H_4NHCCl(OC_2H_5)$.

II. $OC_6H_4NHCCl(OC_2H_5) + HOH \longrightarrow OC_6H_4NHC(OH)OC_2H_5 + HCl$.

III. $OC_6H_4NHC(OH)OC_2H_5 \longrightarrow HOC_6H_4NHCOOC_2H_5$.[3]

A more thorough investigation, for instance, of the reversibility of reaction II is necessary, to make the reactions of permanent value for the theory of the constitution of imidoether salts.

EXPERIMENTAL PART.

Reduction of o-Nitrophenylethyl Carbonate.

Oxyphenylurethane, $HOC_6H_4NHCOOC_2H_5$.—The reduction was carried out at first in alcoholic solution, according to Bender's directions: 27 grams of *o*-nitrophenyl carbonate were dissolved in alcohol, 65 cc. of concentrated hydrochloric acid added, and then slowly 40 grams of powdered tin. The whole was kept cool with ice-water. After three hours the solution was filtered and about an equal quantity of water added. Immediately an oil separated which slowly crystallized on being placed in ice-water. The melting-point of the crystals was 72°–83°. After crystallizing the substance three times from water and then precipitating it from a solution in benzene with ligroin, the melting-point remained constant at 86°. On heating the filtrate, from the oil which first separated, and then allowing it to cool slowly, more crystals sepa-

[1] Stieglitz: This JOURNAL, **21**, 106.
[2] Stieglitz: *Ibid.*, *Loc. cit.*

rated which had the melting-point 85°. If, however, the filtrate was allowed to stand without heating, crystals began to separate only after some hours, and then continued to form for some days. The melting-point was the same in both cases.

A quicker method of carrying out the reduction is to use a concentrated aqueous acid solution: 25 grams of the nitro carbonate are put in a flask with 60 cc. of concentrated hydrochloric acid and very little water, then 40 grams of tin slowly added, and the whole kept cold in ice-water during the first part of the action, it being allowed finally to reach the ordinary temperature. When the solution has become clear (in about forty-five minutes) it is filtered through glass-wool, after the addition of about an equal volume of water, and heated nearly to boiling for a few minutes. An oil separates which, on cooling, becomes a solid mass of crystals. On recrystallizing twice from water the melting-point is 86°.5. If the solution, during reduction, is allowed to become quite warm, mixtures result which melt between 70° and 130°, consisting of oxyphenylurethane (m. p. 86°) and carbonylaminophenol (m. p. 137°). This was proved by separating the mixture, by fractional precipitation, from a solution in benzene by carefully adding ligroin. Incidentally the presence of carbonylaminophenol was shown on treating a sample of oxyphenylurethane, which happened to contain some carbonylaminophenol, with diazomethane. Crystals separated in this case from the methoxyphenylurethane, which is an oil, and these were identified as carbonylmethylaminophenol (m. p. 86°), by comparison with the synthetic compound.

The oxyphenylurethane, prepared as described, crystallizes in rather short, thick needles or plates, varying somewhat with the medium from which it is crystallized. It is soluble in most of the organic solvents except ligroin, somewhat soluble in cold water, much more so in boiling water. It is soluble in cold, dilute, caustic alkalies, from which solution it is precipitated unchanged by acids. The crude crystals (m. p. 72°–83°) deposited from the acid solution invariably dissolved completely in dilute alkali. The change into oxyphenylurethane was, therefore, not effected by the process of purification

but occurred in the original acid solution. From a concentrated solution in the alkalies the potassium and sodium salts crystallize in large needles.

Analyses of oxyphenylurethane, obtained by reduction of *o*-nitrophenylethyl carbonate, gave the following results:

I. 0.2485 gram substance gave 0.5410 gram CO_2, and 0.1371 gram H_2O.

II. 0.3244 gram substance gave 21.5 cc. N at 15.75° and 749.1 mm (corr.).[1]

	Calculated for $C_9H_{11}NO_3$.	Found.
C	59.66	59.35
H	6.07	6.12
N	7.73	7.76

For comparison with Bender's product, oxyphenylurethane was also prepared according to Groenvik's[2] method, by treating *o*-aminophenol (2 mols.) in ethereal solution with ethyl chlorformate (1 mol.). Transparent, thick needles separated out on partial evaporation, and these were recrystallized from hot water. The melting-point was then 86.°5, and in appearance the compound was similar to the substance obtained by reduction of nitrophenylethyl carbonate. Mixtures of the two had the same melting-point as either separately.

Benzoyloxyphenylurethane, $C_6H_5COOC_6H_4NHCO_2C_2H_5$.—In order more fully to establish the identity of the two substances as oxyphenylurethane, the benzoate was obtained from both preparations. Each of the substances was dissolved in a solution of potassium hydroxide (1 mol.). In each case an oil separated which, when shaken, hardened to a crystalline mass. This was recrystallized twice from alcohol, to which a little water had been added. The melting-point of each, as well as that of a mixture of the two, was 75°.5. Both were insoluble in alkalies and acids, very soluble in warm alcohol and most of the organic solvents. About 90 per cent of the theoretical yield was obtained.

I. 0.1696 gram substance gave 7.9 cc. N at 19°.2 C. and 744.7 mm. (corr.).

[1] Corrected for vapor-tension over 30 per cent caustic potash.

[2] Bull. Soc. Chim., **25**, 177.

II. 0.3305 gram substance gave 15 cc. N at 23°.5 C. and 735.3 mm (corr.).

	Calculated for $C_{16}H_{15}NO_4$.	Found. I.	II.
N	4.91	5.35	5.08

Benzoyloxyphenylurethane was also obtained by treating benzoyl-*o*-aminophenol with ethyl chlorformate.

Benzoyl-o-aminophenol, $C_6H_5CONHC_6H_4OH$. — This substance was first made by Hübner,[1] but the following method was found to give satisfactory results: 1 gram (2 mols.) of *o*-aminophenol was suspended in absolute ether, and 0.5 gram (1 mol.) of benzoyl chloride then slowly added to the mixture. A reaction began at once, the hydrochloride of 1 molecule of the base being precipitated, mixed with some of the benzoyl derivative which is not very soluble in ether. The hydrochloride was dissolved out with water, the ether solution washed with dilute hydrochloric acid and water, and the ether then evaporated. The benzoylaminophenol so prepared melted at 165°–167° (with decomposition), was soluble in alkalies, and had all the properties of Hübner's product.

Action of Ethyl Chlorformate on Benzoyl-o-aminophenol.

Three grams of benzoyl-*o*-aminophenol were dissolved in a little more than 1 molecule of potassium hydroxide and 1.5 grams (1 mol.) of ethyl chlorformate added. An oil separated out which solidified when shaken. The substance is very soluble in alcohol and ether, fairly soluble in ligroin (40°–60°), from which it crystallizes in white needles. After three recrystallizations the melting-point was constant at 76°.5.

0.2380 gram substance gave 0.5848 gram CO_2, and 0.1143 gram H_2O.

	Calculated for $C_{14}H_{13}NO_4$.	Found.
C	67.36	67.01
H	5.26	5.33

As the melting-point was so near that of its supposed isomer, obtained from oxyphenylurethane and benzoyl chloride in alkaline solution, and as the appearance of the two was so similar, more of that isomer was made and carefully purified

[1] Ann. Chem. (Liebig), **210**, 387.

by recrystallizing it from ligroin. The melting-point now became 76°.5, and that of a mixture of the two was the same. Neither substance decomposed at the melting-point, which was unchanged after the substance solidified on cooling. The substances obtained from benzoyl chloride and oxyphenylurethane on the one hand, and from benzoylaminophenol and ethyl chlorformate on the other hand, are therefore identical. This unexpected conclusion was confirmed by a study of the saponification products of the two substances.

One gram of benzoyloxyphenylurethane (prepared from benzoylaminophenol) was shaken for an hour with a dilute aqueous solution of caustic potash (2 mols.), warming slightly toward the end. Nearly all went into solution. After acidifying, the mixture was extracted with ether, the ethereal solution shaken out with bicarbonate of soda, dried, and the ether evaporated. After recrystallizing from hot water the residue melted at 83°; mixed with *o*-oxyphenylurethane the melting-point was 84°, and it showed all the properties of this substance. The bicarbonate solution was acidified and extracted with ether, a substance being thus obtained whose odor and melting-point characterized it as benzoic acid.

Some of the benzoyloxyphenylurethane (p. 16) prepared from oxyphenylurethane and benzoyl chloride was saponified exactly as described above, and gave the same products—benzoic acid and oxyphenylurethane, thus confirming the identity of the two substances. Consequently some rearrangement in the molecule of one (or both) of them must have occurred. According to the saponification-products the stable substance is benzoyloxyphenylurethane,

$$C_6H_5COOC_6H_4NHCO_2C_2H_5.$$

The attempt to prepare the two possible isomers was repeated, the solutions being kept below 5°, in the hope that, at this temperature, real isomers might be isolated. The substances, however, were identical in every way with those described above, as proved both by appearance and melting-point as well as by saponification in alcoholic potash, which could be accomplished in one or two minutes. As seen under a microscope, no difference could be distinguished between the crys-

tal forms. Both appeared as small, well-formed prisms with end faces perpendicular to the long axis. Finally, the two substances were prepared at —5°, at once washed with water, acid, and alcohol, and then immediately saponified by means of alcoholic potash. The same saponification-products were obtained, showing that one of the isomers did not change into the other stable modification in purifying it, but in preparing it.

Dry Distillation of Benzoyloxyphenylurethane.

Several grams of the dry substance were heated in an Anschütz distilling flask until the thermometer in the vapor had reached 100° C. The liquid collected in the receiver was then poured off and shown to be alcohol by the iodoform test. The flask was then heated again under somewhat reduced pressure, until crystals began to appear in the neck of the receiver. The liquid in the receiver was again poured off and, by its odor and boiling-point (213°), proved to be benzoic ether. A vacuum was again secured and most of the residue distilled at 200°–220°. A solid distillate collected in the receiver. This was digested some time with caustic soda, and filtered. The filtrate was acidified and extracted with ether. On evaporating the ether a small amount of a very impure substance was obtained, melting at 85°–105°. It was probably impure carbonylaminophenol, but was not further investigated. The larger part of the solid distillate was insoluble in alkali and was washed with acidified water, then with pure water, and finally recrystallized once from alcohol, in which it is soluble with difficulty. Crystals were obtained melting at 174° and possessing all the properties of benzoylcarbonylaminophenol, which will be described presently. When water was added to the mother-liquor from the first crystallization from alcohol, crystals were deposited which were very soluble in alcohol and melted at 97°–101°. Some of the substance, sublimed *in vacuo*, melted at 102°. The crystals were long needles soluble in cold ether and benzene, less soluble in ligroin, somewhat soluble in boiling water, slightly in dilute sulphuric acid, quite soluble also in concentrated hydrochloric acid, reprecipitated by alkalies. It was suspected that this

substance was benzenylaminophenol (m. p. 101°–103°), and this was confirmed by preparing the latter synthetically according to the method described by Ladenburg.[1] The melting-point and properties of the substance were the same as those described above, and a mixture of the two had the same melting-point.

Benzoylcarbonyl-o-aminophenol, $C_6H_5CoNC_6H_4OCO$. — By distilling oxyphenylurethane, alcohol is given off and carbonylaminophenol is formed. As in distilling benzoyloxyphenylurethane alcohol was formed in large quantities, it was concluded that the substance melting at 174° was the corresponding benzoylcarbonylaminophenol. This substance is not described in the literature, so that it became necessary to prepare it synthetically. This was done by treating carbonylaminophenol in alkaline solution with benzoyl chloride:

$$NHC_6H_4OCO + C_6H_5COCl \longrightarrow C_6H_5CONC_6H_4OCO + HCl.$$

Recrystallized from alcohol the substance melts at 174°.

0.2851 gram substance gave 14.8 cc. of nitrogen at 18°, and 730.3 mm. (corr.).

	Calculated for $C_{14}H_9NO_3$.	Found.
N	5.85	5.88

By mixing equal portions of this substance with that formed by distillation (m. p. 174°) the melting-point was not lowered. The two are identical. The products of the dry distillation of benzoyloxyphenylurethane are therefore chiefly alcohol and benzoylcarbonylaminophenol, to a small extent ethyl benzoate and carbonylaminophenol, and finally some benzenylaminophenol. The formation of ethyl benzoate and carbonylaminophenol according to

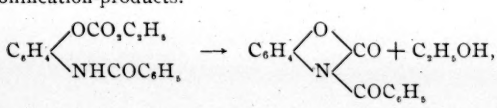
$$C_6H_5COOC_6H_4NHCO_2C_2H_5\ (I) \longrightarrow HNC_6H_4OCO + C_6H_5CO_2C_2H_5,$$

is perhaps in better accord with the constitution assigned to benzoyloxyphenylurethane than with the other possible open-chain form,

[1] Ber. d. chem. Ges., 9, 1526.

$$(C_2H_5O_2C)OC_6H_4NH\overset{*}{C}OC_6H_5\,(II) \longrightarrow HNC_6H_4OCO + C_6H_5COOC_2H_5.$$

The formation of these compounds would involve the separation of carbon atom $\overset{*}{C}$ from nitrogen, which does not occur as easily as from oxygen. But it is particularly worthy of note that the main products of the dry distillation of benzoyloxyphenylurethane are decidedly in better accord with this isomeric form[1] than with the one chosen on the basis of the saponification-products.

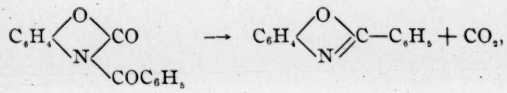


appears as a very simple and likely reaction, but the formation of the same products from

$$C_6H_5CO.O.C_6H_4NHCO_2C_2H_5$$

evidently would involve a much more complicated reaction since the benzoyl group is finally found attached to nitrogen. Much value was attached to this fact in my preliminary report—rightly it seems as long as molecular rearrangements of the diacyl compounds were not to be considered. But since these must take place under much simpler conditions below 0°, their occurrence in the process of dry distillation would not now be surprising. More work, however, has been planned for the study of these conditions. It may be mentioned, in this connection, that the dry distillation of the otherwise analogous *m*-nitrobenzoyloxyphenylurethane does not yield any *m*-nitrobenzoylcarbonylaminophenol. In this case the chief product is *m*-nitrobenzenylaminophenol, corresponding to the decomposition-product obtained from benzoyloxyphenylurethane in smallest quantity—the anhydro base, benzenylaminophenol. The formation of this substance acquires special interest therefrom. It was suspected that it is formed from benzoylcarbonylaminophenol as follows :

[1] Or with the ring form, see preliminary report, *loc. cit.*, p. 1063, and introduction, p. 6.



and it was shown that pure benzoylcarbonylaminophenol, when distilled, does decompose to some extent in the manner indicated. This may account for the fact that, in the case of *m*-nitrobenzoyloxyphenylurethane, as the *m*-nitrobenzoylcarbonylaminophenol disappears from the distilled product, the amount of anhydro base is proportionately increased. But it has also awakened the suspicion that the first action of heat may be to form alcohol and benzoyloxyphenyl isocyanate:[1]

$$C_6H_5COOC_6H_4NHCOOC_2H_5 \longrightarrow C_6H_5COOC_6H_4N{=}CO.$$

This could very well be converted into benzoylcarbonylaminophenol, or lose carbon dioxide, and give benzenylaminophenol. The preparation of this isocyanate will, therefore, be one of the first steps in the further study of these derivatives.

The result of the one case already given, in which the same substance is formed in whatever order the two acyl groups are introduced into the *o*-aminophenol molecule, was so unexpected that its correctness was tested by the use of other acyl radicals, in order to determine whether it holds, in general, for diacyl-*o*-aminophenols. *m*-Nitrobenzoyl chloride being easily available, it was first used in place of benzoyl chloride.

m-Nitrobenzoyloxyphenylurethane, $NO_2C_6H_4COOC_6H_4NHCO_2C_2H_5$, was prepared from oxyphenylurethane and *m*-nitrobenzoyl chloride in alkaline solution. Recrystallized from alcohol it melts at 86°.5.

I. 0.2425 gram substance gave 0.5147 gram CO_2, and 0.1032 gram H_2O.

II. 0.2541 gram substance gave 0.5388 gram CO_2, and 0.0992 gram H_2O.

III. 0.2698 gram substance gave 16.9 cc. N at 18°, and 730.4 mm. (corr.).

IV. 0.2523 gram substance gave 17.3 cc. N at 19°, and 734.9 mm. (corr.).

V. 0.2085 gram substance gave 16.2 cc. N at 20°, and 728.8 mm. (corr.).

[1] *Vide* Hofmann: Ber. d. chem. Ges., **14**, 2727; Folin: This JOURNAL, **19**, 338.

	Calculated for $C_{16}H_{14}N_2O_6$.	Found. I.	II.	III.	IV.	V.
C	58.18	57.88	57.81	....	....	....
H	4.24	4.70	4.32	....	....	....
N	8.48	....	....	7.09	7.78	8.72

In the first two estimations of nitrogen, nitrite was found in the potash solution. Therefore the last analysis was made in a long furnace with the introduction of a spiral of reduced copper 12 to 15 inches in length.

The substance is soluble in alcohol, ether, and benzene, almost insoluble in ligroin, and insoluble in alkalies and acids. By dissolving in benzene and then adding ligroin, very fine prisms are formed.

Three grams of the substance (m. p. 86°.5) were saponified in the cold by alcoholic potash (2. mols.) and the products isolated in the usual manner. They were found to be oxyphenylurethane and *m*-nitrobenzoic acid, having all the properties of the synthetic products. A very small amount of ethyl *m*-nitrobenzoate (m. p. 40°–42°) was also recovered. The only products of the saponification of *m*-nitrobenzoyloxyphenylurethane are, therefore, *m*-nitrobenzoic acid and oxyphenylurethane. To a slight extent ethyl *m*-nitrobenzoate is split from the molecule, exactly as occurs on heating the substance. No *m*-nitrobenzoylaminophenol is formed.

Five grams of *m*-nitrobenzoyloxyphenylurethane (m. p. 86°.5) were heated in a metal bath to 250°–260°, an Anschütz flask being used. Alcohol was driven off, and also a small amount of a solid melting at 80°–123°. The flask was then exhausted and the contents distilled. Some decomposition occurred, giving a slight odor of aniline. About 2.5–2.75 grams of distillate were obtained. This was ground in a mortar with alkali, and filtered. On acidifying the filtrate a small amount of a white solid separated, which proved to be a mixture of *m*-nitrobenzoic acid and carbonylaminophenol. The neutral residue (chief part) was then boiled out with very little alcohol, to remove *m*-nitrobenzoic ether. On adding water to the filtrate a solid separated, which melted at 38°–41°, and proved to be this ether. The greater part was found to be almost insoluble in alcohol, ether, and acetone;

fairly soluble in chloroform and acetic acid, depositing a white solid melting at 203°–205°. Recrystallized from a large amount of absolute alcohol, the melting-point was raised to 207°, resolidifying at 200°. The compound is also soluble in concentrated hydrochloric acid, but is reprecipitated on adding water. Reasoning from the results of the work on the benzoyl derivative, it was thought to be either *m*-nitrobenzoylaminophenol or *m*-nitrobenzenylaminophenol, and was shown to be the latter by comparing it with synthetic preparations of these substances.

m-Nitrobenzoylcarbonylaminophenol, $NO_2C_6H_4CO—NC_6H_4OCO$.—Molecular quantities of carbonylaminophenol and *m*-nitrobenzoyl chloride in caustic soda solution gave this substance. On recrystallizing from alcohol, in which it is very difficultly soluble, it becomes pure white and melts at 199°.5–201°.5, but resolidifies at 180°, again melting at the same temperature as before. Mixed with the substance of melting-point 207°, obtained in the dry distillation of *m*-nitrobenzoyloxyphenylurethane, the melting-point was depressed to 175°–193°, showing that the substances are not identical. It is practically insoluble in ether, ligroin, alkalies, and concentrated hydrochloric acid, somewhat soluble in acetic acid, easily in chloroform. The purity of the substance was controlled by an analysis:

0.1986 gram substance gave 0.4289 gram CO_2, and 0.0545 gram H_2O.

	Calculated for $C_{14}H_8N_2O_5$.	Found.
C	59.15	58.89
H	2.81	3.04

m-Nitrobenzenyl-o-aminophenol, $C_6H_4(NO_2)C=NC_6H_4O$.—This anhydro base was prepared by heating molecular quantities of *o*-aminophenol and *m*-nitrobenzoyl chloride. The residue was difficultly soluble in alcohol, but recrystallized from this solvent in light grayish-yellow crystals of melting-point 207°, resolidifying at 200°. Mixed with the substance having the same melting-point, obtained by distilling *m*-nitrobenzoyloxyphenylurethane, no depression was observed. The

two substances are therefore identical. Mixed with *m*-nitrobenzoylcarbonylaminophenol (m. p. 199°–201°) the melting-point was depressed 25°. The anhydro base is difficultly soluble in most organic solvents, except chloroform, but is soluble in concentrated hydrochloric acid, and is reprecipitated by adding water.

0.1052 gram substance gave 0.2498 gram CO_2, and 0.0346 gram H_2O.

	Calculated for $C_{13}H_8N_2O_3$.	Found.
C	65.00	64.76
H	3.33	3.61

The high-melting product of the dry distillation of nitrobenzoyloxyphenylurethane is, consequently, *m*-nitrobenzenyl-*o*-aminophenol. It is evident, therefore, that in distilling the molecule lost both alcohol and carbon dioxide. Several attempts were made to split off the first alone, by heating to different temperatures, but without success—both coming off at the same temperature, as was proved. The amount of the high-melting substance was always much less than the theoretical. On that account a roughly quantitative experiment was carried out as follows: 4.75 grams were slowly heated in a metal bath to 125°. The loss in weight, 0.2 gram, was apparently a little moisture. Pure, dry air was drawn through the flask into lime-water, but no trace of carbon dioxide was found; nor had the melting-point of the substance changed. Heating was continued until the first indication of decomposition, 195°, and the temperature kept between this and 200° as long as action was visible. A very little oil had distilled, and the presence of alcohol and carbon dioxide was proved. The residue now weighed 4 grams. This was digested with cold alcohol and filtered into a tared beaker. When the alcohol had evaporated the residue weighed 2.63 grams. After boiling out the more insoluble part with a very little alcohol it weighed 0.8 gram, so that a large part was soluble in cold alcohol. The part soluble in cold alcohol was digested with caustic soda and filtered. On acidifying the filtrate a solid was deposited, which, after recrystallization from alcohol and water, was not quite pure, melting at 133°–135°, and proved

to be carbonylaminophenol by the usual tests. The oily residue, insoluble in alkali, solidified on standing, melted at 38°–40°, and gave all the tests for *m*-nitrobenzoic ether. The most insoluble part, as well as that soluble in boiling alcohol, were mixtures melting from 150°–180°. No simple substance could be separated by recrystallization, but on heating them to 250° they were converted into *m*-nitrobenzenyl-*o*-aminophenol (m. p. 207°). It is evident that in the dry distillation of *m*-nitrobenzoyloxyphenylurethane the decomposition into ethyl nitrobenzoate and carbonylaminophenol occurs to a larger degree than in the case of benzoyloxyphenylurethane (page 6). The decomposition reactions, into nitrobenzoylcarbonylaminophenol, and of this into nitrobenzenylaminophenol, seem to occur at the same temperature, so that the anhydro base becomes one of the main products. The theoretical bearing of this has already been discussed (page 8).

As the substance by heat could not be made to lose alcohol alone, a little was dissolved in concentrated sulphuric acid and allowed to stand about five minutes. Then water was added slowly, when a solid separated which was recrystallized from much hot alcohol. The melting-point was 199°–201°, and mixed with *m*-nitrobenzoylcarbonylaminophenol, made synthetically and melting at this point, no depression of the melting-point was observed. We have here again the peculiar fact that the *m*-nitrobenzoyl group is found attached to nitrogen, while the above synthesis and saponification of *m*-nitrobenzoylurethane show it attached to oxygen, unless, indeed the diacyl-*o*-aminophenols have a ring constitution, which the monoacyl derivatives have been proved not to possess (page 9, introduction).

m-Nitrobenzoyl-o-aminophenol, (*m*)-$O_2NC_6H_4CONHC_6H_4OH$. —To 2 grams (2 mols.) of *o*-aminophenol, suspended in ether, an ether solution of 1.7 grams (1 mol.) of *m*-nitrobenzoyl chloride was added. The ethereal filtrate gave a small yield of a substance melting at 207°. The solid which was precipitated in the ether solution was washed with water to remove the hydrochloride of aminophenol. Recrystallized from alcohol, the substance was obtained in short, thick prisms of a light-yellow color, melting at 207°. Nitrobenzoylaminophe-

nol dissolves in alkalies, forming a bright-yellow solution, and is reprecipitated unchanged on addition of dilute acids.

Action of Ethyl Chlorformate on m-Nitrobenzoyl-o-aminophenol.—3.35 grams of the nitrobenzoylaminophenol were dissolved in a little more than the calculated amount (1 mol.) of potassium hydroxide in solution, and 1.5 grams (1 mol.) of ethylchlorformate added. On shaking a solid separated in a somewhat oily condition. It was extracted with ether, but this solution immediately commenced to deposit crystals. The substance was purified by dissolving in benzene and carefully adding ligroin. The melting-point was found to be 86°.5. The yield was quantitative.

0.1335 gram substance gave 0.2845 gram CO_2, and 0.0536 gram H_2O.

	Calculated for $C_{16}H_{14}N_2O_6$.	Found.
C	58.18	58.12
H	4.24	4.42

The substance has the same appearance, crystalline form, and melting-point as its supposed isomer, *m*-nitrobenzoyloxyphenylurethane, and the melting-point of a mixture of the two is the same as that of either, proving the identity of the compounds. This was fully confirmed by the result of saponifying the substance whose preparation has just been described.

Two and three-tenths grams of the substance treated with alcoholic potash, as described for *m*-nitrobenzoyloxyphenylurethane, gave 0.93 gram *m*-nitrobenzoic acid (m. p. 139°–141°) and 1.18 grams oxyphenylurethane, which softened at 79° but melted at 84°. The melting-point was raised a little by mixing with pure oxyphenylurethane. These are the same saponification-products as *m*-nitrobenzoyloxyphenylurethane gives. Again the action of ethyl chlorformate on nitrobenzoyl-*o*-aminophenol,

$$HOC_6H_4NHCOC_6H_4NO_2 + ClCO_2C_2H_5,$$

and of nitrobenzoyl chloride on oxyphenylurethane,

$$HOC_6H_4NHCO_2C_2H_5 + ClCOC_6H_4NO_2,$$

give the same substance which, according to the saponification-products, is *m*-nitrobenzoyloxyphenylurethane,

$$NO_2C_6H_4COOC_6H_4NHCO_2C_2H_5.$$

A molecular rearrangement must then convert the isomer into this same compound.

Diacyl-*o*-aminophenols were also prepared, benzoyl and nitrobenzoyl being used as the two acyl radicals, without any carbethoxy group, particularly in order to determine whether their abnormal behavior—originally in excellent agreement with a ring formation, now considered to be due to rearrangements by means of ring formations—is dependent in any way on the reactivity of the carbethoxy group. The preliminary work indicated a difference of 15° in the melting-points of the two substances, benzoylaminophenol *m*-nitrobenzoate and *m*-nitrobenzoylaminophenol benzoate. By further purification, however, this difference was reduced to hardly 1°. The saponification-products of both substances were repeatedly found to be identical. However, the general appearance and crystalline forms remained persistently so different that I was led to a careful and exact reinvestigation of the reaction under different conditions. The results were the same, so that I shall describe only those conditions which seem to me to be the most favorable for the production and identification of isomeric bodies.

m-Nitrobenzoyl-o-aminophenol Benzoate, $NO_2C_6H_4CONHC_6H_4OCOC_6H_5$.—1.29 grams of *m*-nitrobenzoyl-*o*-aminophenol, freshly made and carefully purified, were dissolved in a solution of sodium hydroxide (1 mol.) at 0°, and 0.7 gram (1 mol.) of cold benzoyl chloride added, the whole being well shaken. The separated solid was filtered, washed with alkali, then thoroughly with water. A little was dried, and without being crystallized it melted at 148°–151°. The rest was washed with cold alcohol; a little dissolved which had the melting-point 151°–153°. Some was recrystallized twice from alcohol; it then melted at 153°.

0.2486 gram substance gave 17.4 cc. N at 22° C., and 726.9 mm. (corr.).

	Calculated for $C_{20}H_{14}N_2O_5$.	Found.
N	7.73	7.78

The crystals were long, white, hair-like needles, not very soluble in alcohol, insoluble in alkalies and acids. 3 grams

of the substance, without crystallization, were treated with alcoholic potash in excess. In one minute all had dissolved, and this was not precipitated on adding water. The solution was acidified immediately, extracted with ether, the extracts washed with water, and a solution of sodium bicarbonate (*B*), dried with calcium chloride, and the ether evaporated. This residue (*A*) containing the monoacylaminophenols was dissolved in alkali and extracted with ether to remove any of the original substance, and again acidified. A solid separated which was recrystallized several times. The melting-point was about 160°, though not sharp. A little was dissolved in alkali and benzoyl chloride added. A solid formed, melting at 178°, 2° above that given for dibenzoyl-*o*-aminophenol. To remove any trace of *m*-nitrobenzoyl-*o*-aminophenol, the monoacylaminophenol was dissolved in alcohol, ammonia added, and hydrogen sulphide passed through the solution to reduce the nitro body. After evaporation the solid residue was washed with acid and water, then recrystallized from alcohol. It now softened at 164°, melting at 165°–167°. Mixed with benzoyl-*o*-aminophenol this was not depressed, showing that (*A*) consisted chiefly of this substance. The carbonate solution (*B*) was acidified and extracted with ether, yielding a substance melting at 139°–141°, and with all the properties of *m*-nitrobenzoic acid. The benzoate of *m*-nitrobenzoylaminophenol gives, therefore, as the chief products of saponification *m*-nitrobenzoic acid and benzoylaminophenol, in which the benzoyl group is attached to nitrogen, in the position originally held by the other acyl radical. Only traces of benzoic acid and *m*-nitrobenzoylaminophenol are formed. The substance was saponified also in warm hydrochloric acid, a little alcohol being used as solvent. The products were the same as those in alkaline solution.

Benzoyl-o-aminophenol-m-nitrobenzoate, $C_6H_4CONHC_6H_4OCOC_6H_4NO_2$.—4 grams of benzoyl-*o*-aminophenol were dissolved in caustic soda, 3.5 grams (1 mol.) of *m*-nitrobenzoyl chloride (in ether) added, and the whole shaken for some time. The separated solid was washed and then recrystallized from alcohol. After the first recrystallization the melting-point was constant at 152°. The crystals be-

ing colored, they were boiled with alcohol and bone-black, filtered, then allowed to crystallize. If heated very slowly the substance now melted at 151°. It was dried at 100° and analyzed.

0.1178 gram substance gave 0.2862 gram CO_2, and 0.0433 gram H_2O.

	Calculated for $C_{20}H_{14}N_2O_6$.	Found.
C	66.29	66.21
H	3.86	4.07

The substance crystallizes persistently in short, thick prisms, quite unlike the hair-like needles described above.

Two grams of the substance were shaken with a solution containing 2 molecules of caustic potash, heat being applied toward the end. Nearly all went into solution. After filtering and acidifying, the solution was extracted with ether, the ether solution washed with a solution of sodium bicarbonate (*B*), and the ether allowed to evaporate. The residue (*A*) containing monoacylaminophenol was boiled with water, then dissolved in alcohol, boiled with bone-black, and filtered. The crystals were then digested with a very little cold ether. Nearly all dissolved, leaving but a small amount of a substance melting at 204°–207°, which was recognized as *m*-nitrobenzoyl-*o*-aminophenol by the fact that a mixture of the two had the same melting-point. The chief part of (*A*), soluble in ether, on further purification softened at 158° and melted at 163°. It is evidently benzoyl-*o*-aminophenol mixed with a trace of the nitro body, but this was not removed as in the former case. The bicarbonate solution (*B*) when acidified and extracted with ether, left a substance melting at 136°–138° and having somewhat the odor of benzoic acid. It has all the properties of *m*-nitrobenzoic acid (m. p. 141°). The chief saponification-products of the *m*-nitrobenzoate of benzoylaminophenol are therefore *m*-nitrobenzoic acid and benzoylaminophenol, the same as those of the benzoate of *m*-nitrobenzoyl-*o*-aminophenol. But, exactly as in the case of the latter, very small quantities of benzoic acid and nitrobenzoylaminophenol are also formed—the latter containing the nitrobenzoyl group attached to nitrogen where the benzoyl group was originally held.

The melting-point of a mixture of benzoyl-*o*-aminophenol-*m*-nitrobenzoate,

$$C_6H_5CONHC_6H_4OCOC_6H_4NO_2$$

(m. p. 152°), and *m*-nitrobenzoyl-*o*-aminophenol benzoate,

$$NO_2C_6H_4CONHC_6H_4OCOC_6H_5$$

(m. p. 153°), was less exact than that of either separately, as it softened slightly at 146° and melted at 149°–153°. The saponification-products are the same but the crystal forms are persistently different. The solubility of the two forms, in alcohol, are 31.16 per cent and 27.5 per cent, respectively. Many attempts were made to change one form of crystals into the other, but under no conditions could more than a trace of the hair-like needles be changed into the prisms, and never any in the opposite direction. The closeness of the melting-points, the identity of the saponification-products,[1] and the fact that by mixing the two substances the depression of the melting-point is very slight, while, as a rule, in this series, such a mixture causes a depression of 15°–20°, raise some doubt as to the isomerism of the two substances. The persistent difference in crystal form and the like difference in solubility, make it very probable, on the other hand, that they are isomers. In that event, however, rearrangement must occur either just before or just after saponification, unless the substances are indeed ring derivatives.

One other attempt was made to obtain more sharply defined isomers of the two diacyl-*o*-aminophenol series by means of phenyl isocyanate. Leuckart has shown[2] that phenyl isocyanate, in the presence of aluminium chloride, unites with the amide group in *o*-amidophenol, but that in substituted *o*-amidophenols the isocyanate reacts with the hydroxyl group:

$$HOC_6H_4NH_2 + C_6H_5NCO \longrightarrow HOC_6H_4NHCONHC_6H_5;$$
$$HOC_6H_4NHCOR + C_6H_5NCO \longrightarrow C_6H_5NHCOOC_6H_4NHCOR.$$

Carbethoxyaminophenol Phenylcarbamate, $C_6H_5NHCOOC_6H_4NHCO_2C_2H_5$, or $C_6H_5NHCONHC_6H_4OCO_2C_2H_5$.—

[1] See p. 36 as to the saponification-products of the two corresponding undoubtedly isomeric diacyl derivatives of methylaminophenol.

[2] J. prakt. Chem., **41**, 301.

Five grams of oxyphenylurethane and a little more than 1 molecule of phenyl isocyanate were mixed in solution in absolute ether, and a small amount of aluminium chloride slowly added. The solution became warm and the odor of hydrogen chloride was noticed. After standing some hours, and being shaken at intervals, an oil settled out. On evaporating the ether, and washing with water and hydrochloric acid, the oil solidified. On dissolving in alcohol a small amount of carbanilide was separated. After recrystallizing several times the melting-point was constant at 116°–118°.

0.1215 gram substance gave 10.5 cc. N at 20°.5 C. and 726.6 mm. (corr.).

	Calculated for $C_{16}H_{16}N_2O_4$.	Found.
N	9.33	9.65

The substance crystallizes in small, nearly white, prisms and is fairly soluble in most of the usual solvents, but is insoluble in alkalies and acids.

Action of Ethyl Chlorformate on Oxydiphenylurea.

Chemically pure oxydiphenylurea[1] (m. p. 167°) prepared according to Leuckart, was dissolved in sodium hydroxide, and ethyl chlorformate (1 mol.) added. An oil separated which was extracted with ether. The ether solution was washed with alkali, water, acid, then again with water until it gave no test for acid. The solution was dried for from fifteen to eighteen hours with fused sodium sulphate and the ether evaporated. It was then put in a vacuum over sulphuric acid for three days. It did not crystallize, nor would it crystallize on being cooled for a day to —10°–30° (cold winter night). It is insoluble in acid and alkalies, easily soluble in most of the organic solvents. As the oil could not be purified by distillation it was analyzed.

0.2867 gram substance gave 18.9 cc. N at 21° C. and 729 mm. (corr.).

	Calculated for $C_{16}H_{16}N_2O_4$.	Found.
N	9.33	7.37

The oil was apparently quite impure, but it is evidently not

[1] Leuckart gives the melting-point at 163°–165°.

identical with the substance just described (m. p. 116°–118°), as it could not be made to crystallize by inoculation with a crystal of that substance. The small amount of the oil that remained was saponified, after standing a couple of months, with the result that, instead oxydiphenylurea, a few crystals of oxyphenylurethane were obtained. This result is as difficult to explain, on the assumption of an unchanged open chain, as those obtained with the other acyl derivatives, but, as with these, it is easily understood by assuming a ring constitution,

$$C_6H_5NHCONC_6H_4OC(OH)OC_2H_5,$$

or a rearrangement of some of the substances before or after saponification.

Acyl Derivatives of Methyl-o-aminophenol.

Of peculiar importance for the determination of the constitution of oxyphenylurethane and the interpretation of the nature of the diacyl derivatives of *o*-aminophenol, has been the study of the corresponding derivatives of *o*-methylaminophenol, $CH_3NHC_6H_4OH$. The replacement of one hydrogen atom by methyl made it possible to determine the seat of acidity in oxyphenylurethane and, preventing a rearrangement of the diacyl compounds, made a close study of the two isomeric series possible. The methylaminophenol necessary for the experiments, I found, can be prepared much more readily by means of carbonylmethylaminophenol than by way of the corresponding thiocarbonylmethylaminophenol.[1]

Carbonylmethylaminophenol,[2] $CH_3NC_6H_4OCO$.—This is best prepared by dissolving carbonylaminophenol in methyl alcohol, in which is dissolved 1 molecule of potassium hydroxide, and heating for two hours with somewhat more than 1 molecule of methyl iodide. By this method 70 per cent of the theoretical yield was obtained and the remainder of the carbonyl body recovered. The best results were obtained by using not more than 5 grams of the carbonyl body for one experiment. It can be purified by repeated crystallization from

[1] Jour. prakt. Chem. [2], **42**, 453.

[2] See Bender: Ber. d. chem. Ges., **19**, 2269; Carbonylethylaminophenol.

ligroin. It is very soluble in most organic solvents, but insoluble in acids and alkalies. It melts at 86°.

0.2347 gram substance gave 19.3 cc. N at 19° and 741 mm. (corr.).

	Calculated for $C_8H_7NO_2$.	Found.
N	9.39	9.42

Preparation of o-Methylaminophenol, $CH_3NHC_6H_4OH$.—Four to five grams of methylcarbonylaminophenol are sealed in a tube with 15–18 cc. of concentrated hydrochloric acid and heated to 180° for one and a half hours. The contents of the tube are then evaporated to dryness. By stopping the evaporation just at the right point, crystals of the hydrochloride can be obtained, but generally there remains a thick, sticky mass, which gradually hardens. By neutralizing this with a solution of sodium carbonate the free base, methyl-*o*-aminophenol, is liberated, as a white solid, in a fairly pure condition, and melts at 88°–90°.[1] The base turns brown on standing in the air, especially when moist.

Benzoylmethyl-o-aminophenol, $C_6H_5CO(NCH_3)C_6H_4OH$.—3.7 grams (2 mols.) of methyl-*o*-aminophenol are suspended in ether and 2.1 grams (1 mol.) of benzoyl chloride added. After shaking for some time, the ether solution is washed and partly evaporated. Crystals are deposited, which, after two recrystallizations from alcohol, melt at 160°–162°. The compound was dried at 105° and analyzed.

0.2845 gram substance gave 15.9 cc. N at 17°.5 C. and 727.5 mm. (corr.).

	Calculated for $C_{14}H_{13}NO_2$.	Found.
N	6.16	6.31

The substance is soluble in alkali and is reprecipitated by acids.

Benzoylmethyl-o-aminophenylethyl Carbonate, $C_6H_5CON(CH_3)C_6H_4OCO_2C_2H_5$. — 4.5 grams of benzoylmethyl-*o*-aminophenol were dissolved in 1 molecule of potassium hydroxide, and then a little more than 1 molecule of ethyl chlorformate added. A semisolid substance separated. This was extracted with ether, and the ether solution washed and

[1] Seidel gives m. p. 80°. See J. prakt. Chem. [2], **42**, 453.

dried. On evaporating the ether an oily, crystalline mass was deposited, which was exceedingly soluble in alcohol, ether, and benzene, fairly soluble in ligroin (40°–60°). From the last solvent long, silky needles, free from oil and melting at 68°, were obtained.

0.3419 gram substance gave 14.4 cc. N at 18°.5 and 736.9 mm. (corr.).

	Calculated for $C_{17}H_{17}NO_4$.	Found.
N	4.68	4.80

One and nine-tenths grams of the substance (not quite c. p.) were shaken one and a half hours with 2 molecules of caustic soda. When nearly all had dissolved it was shaken with ether, to remove any unchanged material, then acidified and again extracted. The ether solution was washed with sodium bicarbonate. On evaporating the ether and recrystallizing the residue from alcohol it melted at 160°–162°, and was identical with benzoylmethyl-*o*-aminophenol. The solution in bicarbonate contained a very small amount of a solid which was not identified.

o-Oxyphenylmethylurethane (*ethyl-o-oxyphenylmethylcarbamate*), $HOC_6H_4N(CH_3)CO_2C_2H_5$.—2.72 grams (2 mols.) of methyl-*o*-aminophenol were suspended in absolute ether; to this was added 1.28 grams (1 mol.) of ethyl chlorformate, and then the mixture was shaken for some time. The ether solution was poured from the hydrochloride of the base, washed, dried, and the ether evaporated. The resulting oil was distilled at reduced pressure (18–20 mm.), nearly all passing over at 175°–180°. The oil did not crystallize in a freezing-mixture of ice and salt, nor on standing a week *in vacuo* in an ice chest. Some months later, when the temperature was −20° to −30°, it was kept for twenty-four hours at this temperature after adding a little ligroin, and thus it was crystallized. On recrystallization it tended to become oily, but I was able, by inoculation, to get a product sufficiently pure to determine the melting-point as 53°. The oil is soluble in alkalies and is reprecipitated by acids. It is separated from a little methylcarbonylaminophenol, formed in distilling, by dissolving in alkali, extracting with ether, acidifying, and again extracting. It was analyzed in the form of its benzoate.

Benzoyl-o-oxyphenylmethylurethane, $C_6H_5COOC_6H_4N(CH_3)CO_2C_2H_5$.—The purified oil was dissolved in sodium hydroxide, 1 molecule of benzoyl chloride added, and the whole shaken for some time. A solid separated, which was purified by recrystallization from alcohol. It melted at 88°–90°.

0.2623 gram substance gave 11.2 cc. N at 18°.5 C. and 725.6 mm. (corr.).

	Calculated for $C_{17}H_{17}NO_4$.	Found.
N	4.68	4.79

The substance crystallizes in nearly white needles, is fairly soluble in most organic solvents, but insoluble in alkalies and acids.

The benzoate, saponified and treated as usual, gave benzoic acid (m. p. 121°, not depressed by an admixture of the acid), and an oil which had all the properties of oxyphenylmethylurethane. The two reactions, between ethyl chlorformate and benzoylmethylaminophenol on the one hand, and between benzoyl chloride and oxyphenylmethylurethane on the other hand, led to two different substances—stable isomers:

$$HOC_6H_4N(CH_3)COC_6H_5 + ClCO_2C_2H_5 \longrightarrow (CO_2C_2H_5)OC_6H_4N(CH_3)COC_6H_5 + HCl,$$

and $$HOC_6H_4N(CH_3)CO_2C_2H_5 + ClCOC_6H_5 \longrightarrow C_6H_5COOC_6H_4N(CH_3)CO_2C_2H_5 + HCl.$$

By saponification each compound loses first the acyl bound to oxygen. A mixture of the two isomers (melting respectively at 68° and 88°–90°) had, of course, no constant melting-point, but it melted partly at 58°, and from this slowly to 80°. The former was much the more soluble in alcohol, and the general appearance of the two was quite different.

m-Nitrobenzoylmethyl-o-aminophenol, $HOC_6H_4N(CH_3)COC_6H_4NO_2$, was prepared from methyl-*o*-aminophenol (2 mols.) and *m*-nitrobenzoyl chloride (1 mol.). The substance is not very soluble in ether. On crystallizing from alcohol beautiful, large, nearly white crystals separated. They melted at 105°, and decomposed at 110°–115°. The sub-

stance is soluble in alkalies. It was analyzed in the form of its benzoate.

m-Nitrobenzoylmethyl-*o*-aminophenol, $HOC_6H_4N(CH_3)COC_6H_4NO_2$ (1.5 grams), was dissolved in sodium hydroxide and somewhat more than 1 molecule of benzoyl chloride added. An oil separated, which solidified with difficulty. On recrystallizing it from alcohol, the crystals were pure white and exceptionally perfect, melting at 141°.

0.3231 gram substance gave 0.7908 gram CO_2, and 0.1227 gram H_2O.

	Calculated for $C_{21}H_{16}N_2O_5$.	Found.
C	67.00	66.76
H	4.25	4.21

One gram of the substance was saponified exactly as in the former cases. The acid part melted at 117°–120°, and, mixed with benzoic acid, this melting-point was not depressed. It also had the odor and other properties of benzoic acid. The other portion, crystallized from ether, melted at 105° and decomposed at 110°. It had all the properties of *m*-nitrobenzoylmethyl-*o*-aminophenol.

m-Nitrobenzoate of Benzoylmethyl-o-aminophenol, $NO_2C_6H_4COOC_6H_4N(CH_3)COC_6H_5$.--Benzoylmethyl-*o*-aminophenol, $HOC_6H_4N(CH_3)COC_6H_5$ (1.75 grams), was dissolved in sodium hydroxide (1 mol.) and *m*-nitrobenzoyl chloride (1 mol.) added. An oil separated which slowly solidified. On recrystallizing it from alcohol, it separated in large, stout crystals melting at 123°.5.

0.2109 gram substance gave 14.5 cc. N at 20°.5 C. and 735 mm.

	Calculated for $C_{21}H_{16}N_2O_5$.	Found.
N	7.45	7.78

The substance is quite soluble in alcohol, ether, and benzene; insoluble in acids and alkalies.

One gram of the substance was saponified, two to three times the calculated amount of alcoholic potash being used. All dissolved in a few minutes, and nothing was precipitated on adding water. The solution was then acidified and treated as in other cases, when it yielded benzoylmethyl-*o*-aminophe-

nol, melting at 159°–161°, and *m*-nitrobenzoic acid, melting at 139°–141°. A mixture of the two isomers, melting respectively at 123°.5 and 141°, melted at 115°. In the diacyl derivatives of methyl*o*-aminophenol, therefore, there is no molecular rearrangement. Both isomers are stable, and by saponification the acyl attached to oxygen is always split off first.

Methylation of Oxyphenylurethane, $HOC_6H_4NHCOOC_2H_5$.—The behavior of the diacyl derivatives of *o*-aminophenol, and particularly of the acylated *o*-oxyphenylurethanes, showed plainly that we were dealing with derivatives of the ring form,

$$\underset{\llcorner\!\!\!

o-Methoxyphenylurethane (*o-Anisidineurethane*), $CH_3OC_6H_4NHCO_2C_2H_5$.—Anisidine was suspended in water, an excess of alkali added, and then one molecule of ethyl chlorformate. An oil was formed, insoluble in acids. It was washed with dilute acid, extracted with ether, and this solution dried. After evaporating the ether the oil was distilled at 25–30 mm. pressure. This distillate was fractionated, when a nearly colorless oil, boiling at 180°–182° under 26 mm. pressure, was obtained.

0.3146 gram substance gave 20.4 cc. N at 18°.5 C. and 733.1 mm. (corr.).

	Calculated for $C_{10}H_{13}NO_3$.	Found.
N	7.18	7.36

o-Methoxybromphenylethylurethane, $CH_3OC_6H_3BrNHCO_2C_2H_5$.—An attempt to brominate the urethane, so as to get a solid derivative, showed that mixtures of two products were formed, one melting at 252°, the other at 102°.5, which it was very hard to purify. The last substance gave figures which corresponded very well with a monobrom derivative of anisidineurethane, but the mixtures were so difficult of separation that it was not thought practical to attempt an identification of anisidineurethane by this method. The substance, melting at 102°.5, was dried over sulphuric acid *in vacuo* and analyzed.

I. 0.2302 gram substance gave 0.3796 gram CO_2, and 0.0997 gram H_2O.

II. 0.3181 gram substance gave 0.5211 gram CO_2, and 0.1298 gram H_2O.

III. 0.1588 gram substance gave 0.2626 gram CO_2, and 0.0652 gram H_2O.

IV. 0.2740 gram substance gave 12.9 cc. N at 18°.5 and 745.4 mm. (corr.).

	Calculated for $C_{10}H_{12}BrNO_3$.	Found.			
		I.	II.	III.	IV.
C	43.79	44.96	44.67	45.08	....
H	4.37	4.82	4.52	4.53	....
N	5.10	....	....	....	5.43

A much more satisfactory identification was based on the change of the urethane into the corresponding urea chloride

by means of phosphorus pentachloride, according to the method of Lengfeld and Stieglitz,[1] as modified by Folin and Stieglitz. The urea chloride was converted into anisidine-urea and anisidinephenylurea, which were easily purified and identified. The reactions are represented thus:

I. $CH_3OC_6H_4NHCOOC_2H_5 + PCl_5 \longrightarrow CH_3OC_6H_4NHCOCl + C_2H_5Cl + POCl_3$;

II. $CH_3OC_6H_4NHCOCl + 2NH_3 \longrightarrow CH_3OC_6H_4NHCONH_2 + NH_4Cl$.

Two and two-tenths grams of anisidineurethane were placed in a distilling flask, and after adding some chloroform and 2.33 grams (1 mol.) of phosphorus pentachloride the mixture was warmed on a water-bath to 50°–55° as long as a gas (ethyl chloride) was evolved. Then the contents of the flask were cooled and dry hydrogen chloride passed through the solution until the chloroform and most of the phosphorus oxychloride were evaporated. More chloroform was added and again evaporated. Without attempting to purify the urea chloride it was converted into the urea by pouring it into a concentrated solution of ammonia. Immediately an amorphous solid, which was very soluble in alcohol, separated, but on adding water to the alcoholic solution a crystalline substance, which melted at 130°–140°, separated. On boiling it with ligroin, in which it was insoluble, then recrystallizing it from water again, and finally from chloroform and ligroin, the melting-point became constant at 143°–145° (Beilstein gives m. p. 146°.5). It was identical with the urea made from anisidine hydrochloride and potassium isocyanate.

o-Anisidinephenylurea, $(CH_3O)C_6H_4NHCONHC_6H_5$.—0.61 gram of anisidine and 0.59 gram of phenyl isocyanate were mixed in a small beaker, cooled with water. On stirring the mass a thick, heavy oil formed. When the reaction was ended dilute hydrochloric acid was added, which caused the oil to solidify. The urea is soluble in alcohol, ether, and chloroform, almost insoluble in ligroin (40°–60°). Recrystallized from alcohol, it melts at 144°. Dissolved in chloro-

[1] This JOURNAL, **16**, 70.

form and precipitated with ligroin, it crystallized in thick prisms with the same melting-point.

0.2709 gram substance gave 28 cc. N at 22° and 736.8 mm. (corr.).

	Calculated for $C_{14}H_{14}N_2O_2$.	Found.
N	11.66	11.65

On heating a little on platinum foil a strong odor of isocyanate was noticed.

The urea chloride of anisidine was again made, as before described, from the urethane, and then poured into an excess of pure aniline. A heavy, thick oil formed, mixed with a solid. It was washed with dilute acid and water, the oil extracted with ether, and the ether evaporated. The thick oil which remained refused to crystallize even when scratched with a glass rod, and allowed to stand *in vacuo* for several days. But on rubbing into the oil, moistened with alcohol, a crystal of the synthetic urea, it became crystalline immediately. It was recrystallized from alcohol, then from chloroform and ligroin. The crystals now softened at 141° and melted at 142°–144°. Mixed with the synthetic urea the point of fusion was raised slightly. When heated on platinum foil the isocyanate odor became distinctly perceptible.

Methylation of o-Oxyphenylurethane with Diazomethane.— The diazomethane was prepared from nitrosomethylurethane according to the method of Von Pechmann.[1] The methylamine was prepared from acetamide[2] according to Hofmann's method. Nitrosomethylurethane was prepared by following the description of Von Pechmann,[3] the ethereal solution of the urethane being placed in the separating-funnel in which it was to be washed and dried. In this way I avoided entirely the disagreeable effects experienced by this experimenter.

One and eight-tenths grams of oxyphenylurethane were

[1] Ber. d. chem. Ges., **28**, 855.

[2] As no details could be found of the methods employed for making acetamide from ammonia and acetic ether, experiments were carried out to determine the conditions for obtaining the best yield. By mixing 100 grams of the ether with 200 cc. of concentrated ammonia (sp. gr. 0.90), and allowing the mixture to stand until it had become homogeneous (two days), and then distilling, 75–80 per cent of the theoretical amount was obtained.

[3] *Loc. cit.*

dissolved in a small amount of ether, and to this solution was added diazomethane dissolved in ether. The whole was then warmed on the water-bath for an hour, a reflux condenser being used. The yellow color of the solution nearly disappeared and a gas (nitrogen) was evolved. More diazomethane was added and it was again warmed. When the color of the solution remained light-yellow, which showed a slight excess of diazomethane, the ether solution was washed with sodium hydroxide, then with hydrochloric acid and water. On drying and evaporating the ether an oil remained, insoluble in acids and alkalies. It is somewhat viscous, possesses a pleasant, ethereal odor, and is soluble in most of the organic solvents. It could not be made to crystallize in the cold, but was identified as *o*-methoxyphenylethylurethane,

$$CH_3OC_6H_4NHCO_2C_2H_5,$$

by converting it into methoxyphenylurea and methoxycarbanilide by treatment with phosphorus pentachloride, followed by ammonia or aniline, as described above for the synthetic urethane. 0.7 gram of the urethane was thus converted into the urea. A little oil separated, which soon solidified. After filtering it off the solution was evaporated to dryness. The solid residue was dissolved in chloroform, and ligroin carefully added. Transparent crystals formed which, after several recrystallizations, were of a light-brown color, and melted at 145°, softening a little at 140°–142°. Mixed with the urea (m. p. 143°–145°) made from anisidine urethane, the melting-point was not depressed. The crystal forms, as seen under the microscope, were the same, proving conclusively that the two substances are identical.

More of the urea chloride of the methylated urethane was made as already described, and poured into an excess of aniline. A thick oil was formed, which was washed with dilute acids and water. On rubbing the oil with a crystal of the synthetic urea it became a solid mass of crystals. These were purified by recrystallizing from chloroform and ligroin. The substance melted at 144°, and, mixed with the synthetic phenylurea, the melting-point was not depressed. On heating some of the substance on platinum foil, the isocyanate

odor was easily perceptible. The methylated oxyphenylurethane is undoubtedly an anisidine derivative, and therefore *o*-oxyphenylurethane must contain a phenol hydroxyl group.

o-Aminophenylethyl Carbonate, $H_2NC_6H_4OCO_2C_2H_5$.—Having established the fact that a rearrangement occurs when *o*-nitrophenyl carbonate is reduced with tin and hydrochloric acid, and that oxyphenylurethane was the only product thus far liberated, it seemed of interest to isolate the free aminophenyl carbonate, which must be the first product of the reduction, as that might throw some light on the mechanism of the rearrangement. After some unsuccessful attempts, the following method was found to give satisfactory results:

Four grams of *o*-nitrophenyl carbonate are put in a flask with 15 cc. of concentrated hydrochloric acid and cooled in ice-water. To this is added powdered tin in small portions and the whole shaken, the temperature being kept near 0°. If the solution is kept sufficiently cold, almost immediately after becoming clear a fine, white, crystalline solid begins to appear. This contains both organic and inorganic material and is probably a double salt. When no more crystals form, the contents of the flask are poured slowly into a well-cooled solution of 50 grams of potassium hydroxide in 50 cc. of water. If too much heat is allowed to develop at this stage the results are negative. The alkaline solution is immediately extracted six times with ether, a sufficient amount of water being added during the last extractions to dissolve the potassium chloride. The ether solution is washed with water and then dried with solid potassium hydroxide. When dry, the ether is poured off and dry hydrogen chloride passed into it. A copious, white precipitate of the hydrochloride of *o*-aminophenylethyl carbonate is formed which can be filtered and dried on a clay plate. It is stable at the ordinary temperature, and remains perfectly white. From 60–70 per cent of the theoretical yield is obtained. It melts at 150°–152° with evolution of much gas. It is very soluble in cold water and in alcohol. Sodium carbonate decomposes it, forming aminophenylethyl carbonate, an oil which is soluble in dilute acids. On heating an aqueous solution of the salt it becomes cloudy

before the boiling-point is reached, and an oil separates which gradually solidifies on cooling. On recrystallizing this solid from somewhat diluted alcohol, crystals are formed which melt at 85°–86°.5, and resemble oxyphenylurethane. When these crystals are mixed with oxyphenylurethane the melting-point is not depressed. It is also soluble in alkalies and is reprecipitated by acids. A nearly saturated solution of the hydrochloride of *o*-aminophenylethyl carbonate was made, and to this a concentrated solution of platinic chloride was added. After a few minutes, yellow crystals formed. They were somewhat soluble in water and alcohol, insoluble in ether. They were washed with ether in which was some alcohol, dried and analyzed.

0.0446 gram chlorplatinate gave 0.01125 gram of platinum.

	Calculated for $C_{18}H_{24}N_2O_6PtCl_6$.	Found.
Pt	25.16	25.22

0.1664 gram of the hydrochloride was titrated with tenth-normal silver nitrate, potassium chromate being used as indicator. 7.7 cc. of the solution were required.

	Calculated for $C_9H_{13}NClO_3$.	Found.
Cl	16.32	16.42

Some of the salt was put into a separating-funnel with ether and a solution of sodium carbonate added to alkaline reaction. The ether solution was then washed, dried with fused potassium sulphate, and the ether evaporated *in vacuo*. Aminophenylethyl carbonate remained as a basic oil, which was easily soluble in dilute acids and could be converted back into the hydrochloride and the chlorplatinate of *o*-aminophenylethyl carbonate. It was kept over sulphuric acid. After twelve hours it had changed to a crystalline solid which melted at 86°, and it was now soluble in alkalies and was reprecipitated by acids. All the properties of this solid, as well as the melting-point of a mixture with oxyphenylurethane, proved it to be this substance.

In an attempt to convert the hydrochloride of aminophenylethyl carbonate into the corresponding urea, 0.3 gram of the hydrochloride was dissolved in water and a solution of potas-

sium isocyanate added. An oil separated which was dissolved in water, and, on standing some hours, crystals melting at 86° separated, which proved to be oxyphenylurethane. Another attempt was made, an alcoholic solution of the salt being used, but it was converted into the urethane, as in the former experiment. Evidently the rearrangement takes place rather than the usual addition to isocyanic acid.

One gram of the hydrochloride was treated with an ice-cold solution of 2 molecules of sodium hydroxide and a little more than 1 molecule of benzoyl chloride added. The solution was then extracted with ether several times. The residue, left on evaporating the ether, was again digested with very little ether, which dissolved all but a little, and this, recrystallized from alcohol, melted at 180°, and, mixed with dibenzoylaminophenol, did not melt lower.[1] The ether solution deposited crystals which, after one recrystallization from ligroin, melted at 76° and in its crystal form as in its other properties, was identical with the benzoyl derivative of oxyphenylurethane. A mixture of the two had the same melting-point.

In a second attempt to prepare the isomer of the latter compound a little more than 1 gram of the hydrochloride, corresponding to 0.9 gram (2 mols.) of the free base, was put in a separating-funnel with ether and then treated with an excess of sodium carbonate. The ether solution of the free base was washed, dried with solid potassium hydroxide, and then 1 molecule of benzoyl chloride added. After a minute the hydrochloride of 1 molecule of the base separated. This was filtered out, the ether washed with alkali, then with dilute acid, finally with water, and dried with calcium chloride. On distilling the ether a solid remained which melted at 76°. Mixed with the benzoyl derivative of oxyphenylurethane, the melting-point was not depressed.

In order to compare the behavior of aminophenylethyl carbonate towards dilute acid, with that of ethoxymethenylaminophenol,

$$O—C_6H_4N=C—OC_2H_5,$$

[1] Hübner gives 176° as the melting-point of this derivative.

1 gram of the hydrochloride was allowed to stand twenty-four hours with less dilute hydrochloric acid than was sufficient to dissolve all of it. Then it was completely dissolved in this reagent. After standing some days longer, the solution was divided into two portions and one was extracted with ether. On evaporating the ether a solid remained, which, after one recrystallization from water, melted at 70°–119°. The other portion, on standing longer, deposited crystals which melted at 70°–80°, but when mixed with oxyphenylurethane, the melting-point was raised a little. Decomposing this by distilling some of it into the upper part of a test-tube the melting-point was raised to 135°–137°, which proved the sublimate to be carbonylaminophenol. It is quite certain that the original product is a mixture of oxyphenylurethane and carbonylaminophenol, as I have found that mixtures of these, in different proportions, have melting-points anywhere between 70° and 120°. By distillation they give pure carbonylaminophenol.

Action of Hydrochloric Acid on Ethoxymethenyl-o-aminophenol.—In the reduction of the *o*-nitrophenyl carbonate it was thought possible that the hydrochloride of the anhydro base, ethoxymethenylaminophenol, might be formed[1] instead of the amino base. A comparison of this base with aminophenyl-ethyl carbonate was, therefore, undertaken. Some of the anhydro base, obtained through the kindness of Dr. H. N. McCoy, was dissolved in absolute ether and dry hydrogen chloride passed into the solution. The first bubbles produced a crystalline deposit, but this immediately disappeared, and, on evaporating the ether, only carbonylaminophenol remained. The experiment was repeated in dry ligroin solution at —11°. A solid separated which was stable at that temperature, but when put on a clay plate in a cold room the crystals began to decompose, giving off a gas (ethyl chloride) which burned with a green flame. On the clay plate there remained pure carbonylaminophenol (m. p. 136°–138°).[2] The behavior of this

[1] As in Böttcher's experiments with *o*-nitrophenylbenzoate.

[2] This is the typical behavior of the hydrochloride of an imido ether which ethoxymethenylaminophenol hydrochloride represents:

Attention may be called to the unusually low temperature at which the salt decom-

base is therefore different from that of the amino base formed by reducing *o*-nitrophenyl carbonate. And this fact, coupled with the observation already given, that the amino base on standing is converted into the urethane while the anhydro base is stable in ordinary moist air, proves conclusively that the latter is not an intermediate product in the intramolecular rearrangement.

For reasons stated in the introduction (p. 9), it was thought desirable to compare the behavior of the anhydro base toward dilute hydrochloric acid with that of aminophenylethyl carbonate (see above). The anhydro base was allowed to stand several days in contact with dilute hydrochloric acid. The oil gradually disappeared and was replaced by white crystals. When all the oil had disappeared the crystals were filtered off, recrystallized from water, and dried. They melted at 70°–80°, were soluble in alkali, and reprecipitated by acids. On distilling into the upper part of a test-tube and then recrystallizing from water, in which was a little alcohol, a substance melting at 136°–138° was obtained, which proved to be carbonylaminophenol. The low-melting substance is certainly a mixture of oxyphenylurethane, and carbonylaminophenol. The products formed are identical with those obtained by allowing the hydrochloride of aminophenyl carbonate to stand in an acid solution.

p-Nitrophenyl Carbonate, $NO_2C_6H_4OCOOC_6H_5$.—The peculiar rearrangement observed on reducing *o*-nitrophenyl carbonate in the usual way, by which *o*-oxyphenylurethane results, suggests a comparison of corresponding derivatives in the meta or para series, preferably the para series, as that is the more susceptible to molecular rearrangement, and usually resembles the ortho series more than the meta series does.

Ten grams of *p*-nitrophenol were treated with excess of potassium hydroxide, and somewhat more than 1 molecule of

poses. It recalls the behavior of the hydrochloride of ethylphenylimidochlorformate, $ClC(NC_6H_5)OC_2H_5$, which, decomposing below −15° into ethyl chloride and chlorformanilide, could not be isolated by Lengfeld and Stieglitz,[1] although its formation was clearly indicated and formed an important link in their arguments. The properties of the solid hydrochloride of ethoxymethenylaminophenol fully support their assumption of such an intermediate hydrochloride.

[1] This JOURNAL, **16**, 73.

ethyl chlorformate was added in small portions, while the contents were vigorously shaken. A quantitative yield of a nearly white solid melting at 68° was obtained.

0.2533 gram substance gave 14.8 cc. N at 17° and 736.8 mm.

	Calculated for $C_9H_9NO_5$.	Found.
N	6.63	6.71

The carbonate is soluble in ligroin, ether, alcohol, and somewhat in boiling water, from all of which it crystallizes in long, white needles.

Synthesis of p-Nitrophenylethyl Carbonate.

In order fully to establish that in *p*-nitrophenyl carbonate the carbethoxy group is attached to phenol oxygen and not to the nitro group, a synthesis from phenylethyl carbonate was carried out. The phenyl carbonate was cooled to 0° in ice-water and then poured slowly into ice-cold, fuming nitric acid. On pouring the mixture into water a nearly white, crystalline solid separated immediately. If allowed to stand for some time in the strong nitric acid the product is much more impure. On recrystallizing from alcohol it crystallizes well and melts at 68°. A mixture of this with the carbonate made from *p*-nitrophenol has the same melting-point as either, and the two are identical in all their properties.

p-Aminophenylethyl Carbonate, $H_2NC_6H_4OCO_2C_2H_5$.—Several attempts were made to reduce the carbonate with tin and hydrochloric acid, in aqueous and in alcoholic solution, but the yields in each case were small owing to the fact, afterwards discovered, that the base is somewhat soluble in water and is not extracted with ether completely. The best results are secured by proceeding as follows:

Two grams of the nitrocarbonate were dissolved in warm alcohol, concentrated hydrochloric acid added, and then slowly, and in small portions, 11 grams (6 mols.) of stannous chloride. The solution became light-yellow. After fifteen minutes a drop gave no precipitate with water. The whole was then diluted and hydrogen sulphide passed into the solution, until all the tin was thrown down. After filtering, the solution was concentrated *in vacuo* at 50°–55°. On standing,

white crystals of the hydrochloride of *p*-aminophenylethyl carbonate were deposited. The yield was 70 per cent. The crystals are very soluble in water. From dilute solutions caustic alkalies do not precipitate the base. From fairly concentrated solutions sodium hydroxide or sodium carbonate precipitates an oil which solidifies on standing and then melts at 36°. On recrystallizing it an oil, which solidifies only on standing some days, is formed at first. Both crystals and oil dissolve in acid. The base is somewhat soluble in water, gives no purple color with ferric chloride, and does not become colored in the air. On heating the hydrochloride it darkens at 160° and melts at 197° with violent decomposition.

0.2005 gram of the hydrochloride dissolved in water and titrated with tenth-normal silver nitrate, potassium chromate being used as indicator, required 9.3 cc. of the nitrate solution.

	Calculated for $C_9H_{12}NO_2Cl$.	Found.
Cl	16.32	16.46

The platinum salt was made in aqueous solution by precipitating with chlorplatinic acid, washing the precipitate with alcohol and ether, and then drying *in vacuo* over sulphuric acid.

0.2869 gram substance gave 0.0722 gram Pt.

	Calculated for $(C_9H_{12}NO_2)_2PtCl_6$.	Found.
Pt	25.16	25.16

It is a bright-yellow, crystalline solid melting at 237°, blackening at 208°.

p-Ureidophenylethyl Carbonate, $NH_2CONHC_6H_4OCOOC_2H_5$. —The paraminophenylethyl carbonate can also be identified easily by converting it into its urea. 0.3 gram of the hydrochloride was dissolved in a little water and the calculated amount of potassium cyanate added. An oil separated which soon became crystalline. On crystallizing once from hot water it was nearly white and melted at 147°–150°. It is insoluble in alkalies.

All attempts to cause a rearrangement of *p*-aminophenylethyl carbonate to *p*-oxyphenylurethane were unsuccessful. One gram of the hydrochloride was dissolved in water, and,

after the addition of some hydrochloric acid, the solution was allowed to stand two days. No change having taken place, apparently, the solution was boiled two and a half hours under a reflex condenser. It was then allowed to stand a week. The solution was then evaporated at 50°–60° *in vacuo* in an atmosphere of hydrogen sulphide. The residue was washed with a little water, filtered, and tested as follows:

Ferric chloride produced a deep-purple color, due to *p*-aminophenol. Sodium carbonate produced a solid which gradually turned brown on standing. A urea, made as in the former experiment, melted at 167°, blackening at 162° (*p*-oxyphenylurea melts at 167°). It was quite soluble in alkalies. Mixed with the urea of *p*-aminophenyl carbonate (m. p. 147°–150°), the melting-point became 130°–150°. Evidently the acid had caused a saponification of the hydrochloride of *p*-aminophenylethyl carbonate to that of *p*-aminophenol.

Another gram of the hydrochloride of *p*-aminophenylethyl carbonate was dissolved in water and allowed to stand at the temperature of the room for a week. The solution was then evaporated as was the first portion. Ferric chloride gave a very light-purple color. Sodium carbonate precipitated an oil which became solid on inoculating it with a crystal of *p*-aminophenyl carbonate. The oil dissolved in hydrochloric acid. The urea was made as in the former case. It softened slightly at 142°, melting at 146°–148°. Mixed with a synthetic *p*-ureidophenylethyl carbonate, the melting-point was not lowered. It was insoluble in alkalies. No change had occurred. A third portion of the hydrochloride was dissolved in water and alcohol, allowed to stand a week, and then treated as in the former case.

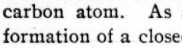
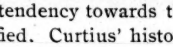
Ferric chloride gave a reddish-purple color. Sodium carbonate separated an oil which gave tests corresponding to *p*-aminophenyl carbonate and formed the same urea. It is evident from these tests that *p*-aminophenylethyl carbonate exhibits no tendency to change into a urethane corresponding to *p*-oxyphenylurethane.

I wish here to express my thanks to Professor Stieglitz for valuable suggestions and for the careful attention he has given to each step of this work.

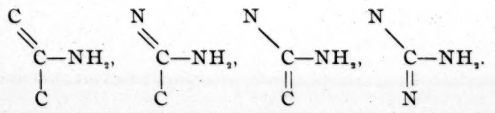
DIAZOCAFFEINE.

By M. Gomberg.

Such few of the aliphatic amines as yield diazo derivatives at all have the amido group linked to a primary or secondary carbon atom. As a consequence the tendency towards the formation of a closed ring is easily satisfied. Curtius' historical diazoacetic ester[1] has the constitution

A similar constitution is ascribed to the esters of diazopropionic[2] and diazosuccinic[3] acids, diazoacetonitril,[4]  , as well as to the diazomethane itself,  .

There is, therefore, a wide difference between these diazo compounds and those of the aromatic series. The first cannot combine with phenols and amines to form azo dyes, while the latter always do so. No diazo derivatives have been prepared of aliphatic amines in which the amido group is linked to a tertiary carbon atom whose three valencies are taken up by three radicals. Some heterocyclic amines, however, with a tertiary carbon atom, have been diazotized, and the derivatives so obtained closely resemble those of the purely aromatic series in their capacity for coupling with phenols and amines. In all such heterocyclic amines the carbon atom carrying the amido group has a linking similar to that in the aromatic amines:

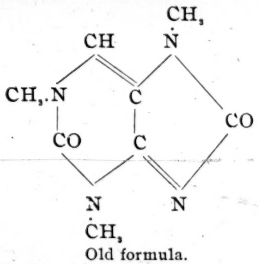


Aromatic. Heterocyclic.

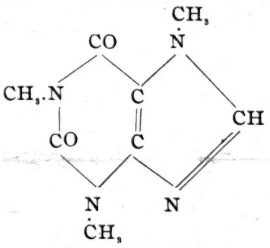
[1] Curtius: J. prakt. Chem. [2], **38**, 396.
[2] Curtius and Koch: *Ibid.*, 487.
[3] Curtius and Koch: *Ibid.*, 474.
[4] Curtius: Ber. d. chem. Ges., **31**, 2489.
[5] Von Pechmann: *Ibid.*, **27**, 1888.

Not all heterocyclic amines of the above constitution can, however, be diazotized. Only very few have yielded such derivatives, and in some cases the diazo salts were not isolated in the dry state, but could exist only in solution. Amidotetrazol,[1] diamidophenylosotriazol,[2] amidotriazol,[3] as well as its methyl and carboxy derivatives, are the most important examples of heterocylic amines that have been successfully diazotized.

Caffeine, although usually looked upon as an aliphatic compound, behaves in many of its reactions more like an aromatic body. Its halogen substitution derivatives part with the halogen with great difficulty; ammonia acts upon them only at a comparatively high temperature and pressure, while zinc ethyl[4] does not act at all at a temperature of 120°–130° C. Caffeine, like all other ureides, can be looked upon as a heterocyclic compound. Its constitution from this standpoint is that of a naphthalene-like combination of a methylated pyrimidine and glyoxaline rings:



Old formula.



Recent formula.[5]

It is therefore not strange that amidocaffeine, with the amido group linked to the tertiary carbon atom, should give a diazo compound on treatment with nitrous acid, even if the amine itself is a very weak base.

Diazocaffeine is a very unstable substance, and so far has been obtained only in solution; even in that form it could be

[1] Thiele and Marais: Ann. Chem. (Liebig), **273**, 144; **287**, 244.
[2] Thiele and Schleusner: *Ibid.*, **295**, 150.
[3] Thiele and Manchot: *Ibid.*, **303**, 40, 50, 54.
[4] Gomberg: This JOURNAL, **14**, 616.
[5] E. Fischer: Ber. d. chem. Ges., **30**, 553.

kept without decomposition at a comparatively low temperature only. It possesses a very great tendency to combine with aromatic phenols and amines. The beautiful azo dyes so formed are quite stable, and are of intense dyeing power. The following few typical examples are described in this paper: Caffeineazophenol, caffeineazodimethylaniline, caffeineazophenylenediamine, and caffeineazo-β-naphthol.

That the caffeine molecule is not broken up by the action of nitrous acid, but that a true diazo salt of caffeine is formed, has been proved in two ways. First, if caffeine instead of its amido derivative is subjected to the same treatment with nitrous acid, it remains entirely unchanged. Second, the azo dyes (the dimethylaniline compound, for instance) on treatment with stannous chloride, furnish almost quantitatively amidocaffeine and the corresponding aromatic body:

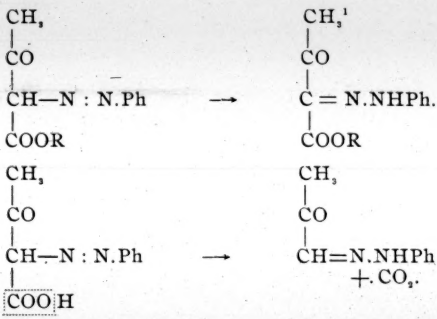
$$C_8H_9N_4O_2.N : N.C_6H_4N(CH_3)_2 + 4H = C_8H_9N_4O_2.NH_2 + H_2N.C_6H_4.N(CH_3)_2.$$

Diazocaffeine couples readily not only with a large number of aromatic compounds but with aliphatic as well. It combines with acetoacetic ester and the free acid, with their homologues, with nitroethane, nitropropane, etc.

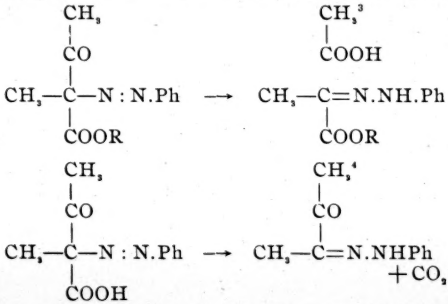
Ever since V. Meyer's[1] discovery of the action of diazobenzene upon acetoacetic ester, this same question has been repeatedly the subject of investigations. The derivatives obtained by this reaction are no longer looked upon as azo bodies,—a view originally entertained by the discoverer,—but rather as hydrazones. This change of view as to the constitution of these and all analogous bodies is due especially to the work of R. Meyer,[2] of Japp and Klingemann,[3] and to the more recent investigations of Bamberger and of Von Pechmann upon the constitution of the formazyl derivatives. It has been established that whenever a diazo salt combines with an aliphatic compound containing a methylene or a methine group, made negative by carbonyl or nitro groups, the derivatives so obtained do not possess the expected azo constitu-

[1] Ber. d. chem. Ges., **10**, 2075.
[2] *Ibid.*, **21**, 118; **24**, 1241.
[3] Ann. Chem. (Liebig), **247**, 190.

tion, but suffer an intramolecular change to the hydrazones:



So great is this tendency to change into hydrazones, that if an *alkyl* acetoacetic ester is employed in this reaction then one of the two negative groups—the acetyl or the carboxyl, depending upon the conditions of the experiment—is entirely split off in order to allow the formation of such a hydrazone:[2]



The recent investigations of Bamberger,[5] Von Pechmann,[6]

[1] Bülow, in a recent article (Ber. d. chem. Ges., **32**, 197) still maintains that in case of acetoacetic ester and some diazo salts true azo bodies result. A similar constitution is ascribed by him to benzoylacetone. *Ibid.*, 2637.

[2] Bülow's diacetylsuccinic ester seems to form an exception to this rule. Ber. d. chem. Ges. **32**, 2880.

[3] Japp and Klingemann: Ann. Chem. (Liebig), **247**, 208.

[4] *Ibid.*, **247**, 218. Also, for instance, in the action of diazobenzene upon camphoric acid (Betti: Ber. d. chem. Ges., **32**, 1995).

[5] Bamberger and Wheelright: Ber. d. chem. Ges., **25**, 3201; Bamberger: *Ibid.*, 3547.

[6] *Ibid.*, **25**, 3175.

Claisen,[1] and Wislicenus[2] show, however, that under certain conditions a second diazo molecule can be introduced into these and similar compounds, and a class of bodies—the formazyl derivatives—is obtained which contain both the hydrazone and the azo constitution. In case of acetoacetic ester we get either acetylformazyl, $CH_3CO.C\begin{matrix}=N.NH.Ph\\ \diagdown N:N.Ph\end{matrix}$, or formazylformic ester, $C\begin{matrix}=N.NH.Ph\\ \diagdown N:N.Ph\end{matrix}—COOR$, the nature of the product being governed by the conditions of the experiment. In presence of a large excess of alkali, even a third molecule of the diazo compound can be introduced, and thus only one carbon atom is left of the whole chain of the acetoacetic ester:

$$C_6H_5N : N.C\begin{matrix}=N.NH.C_6H_5\\ \diagdown N : N.C_6H_5\end{matrix}.$$ [3]

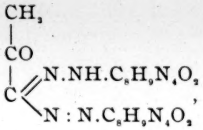
It is unnecessary to enter here in detail upon the behavior of the formazyl derivatives, so thoroughly studied by Bamberger, Von Pechmann, and especially by Wedekind.

The body which I have obtained by the action of diazocaffeine upon acetoacetic acid resembles in appearance so strongly the formazyl compounds, that at first thought it was taken for such. It was considered rather unusual that a formazyl-like body should be formed to such a large extent in an acid solution, especially when the acetoacetic acid was always in excess. Instead of a pale to an orange-yellow hydrazone a body of dark-blue to violet color was obtained in every instance, with a beautiful metallic luster and having the appearance either of fuchsin or of methyl-violet. It possesses intense coloring properties and shows characteristic color reactions in cold and hot water, not unlike those peculiar to cobalt salts. The results of elementary analysis of several samples point, however, to a formula different from what a

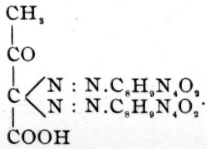
[1] Ber. d. chem. Ges., **25**, 746. [2] *Ibid.*, **25**, 3453.

[3] This benzeneazoformazyl is the end-product of the action of diazobenzene upon a large number of compounds containing either the $CH_3.CO$ group, or the CH_2 group linked to two negative radicals which can be split off more or less readily by hydrolysis.

caffezyl body would require. Instead of the caffezylmethyl-ketone,

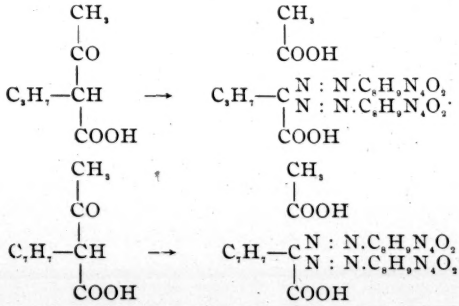


the analytical results point rather to a disazo body:



Such a reaction has, to my knowledge, been observed only once.[1]

Propyl and benzylacetoacetic acids were next taken for this reaction, with the expectation that in this case monoazo bodies would result. But here, too, judging from the results of analysis, disazo compounds were formed, at the expense of the acetyl group:



All these dyes, while not at all, or only slightly, soluble in water, dissolve in dilute alkalies, even in solutions of sodium carbonate, a fact which points to the presence of a carboxyl

[1] Unfortunately, the exact reference has escaped me for the present.

group. While they dissolve in concentrated sulphuric acid, some with reddish, and some with yellowish-green color, none, however, gives on the addition of ferric chloride or of potassium dichromate the blue or violet of Bülow's reaction, so characteristic of all the hydrazones and consequently of the formazyl derivatives. And yet, notwithstanding all these facts, I should still be of the opinion that we have here to deal with formazyl-like bodies had it not been for the following consideration :

Bamberger[1] has shown that the constitution assigned by V. Meyer to the so-called mixed nitroazoparaffins is correct only in cases in which the diazo molecule is linked to a tertiary carbon atom. In all other cases they, too, must be considered as hydrazones.[2] Thus, nitroethane forms $CH_3C(NO_2)(N.NH.Ph)$, while *i*-nitropropane gives, under similar conditions,

$$CH_3C(CH_3)(NO_2)(N:N.Ph).$$

And as the NO_2 group, unlike the acetyl or the carboxyl, cannot be split off under the conditions of the experiment,[3] it follows that of all the nitroparaffins nitromethane alone can give rise to formazyl derivatives. In fact, nitroformazyl, $NO_2—C(N.NH.Ph)(N:N.Ph)$, is the principal product of the interaction of diazobenzene and nitromethane. The yellow hydrazone can be obtained only by observing special precautions.

Diazocaffeine, however, gives in alkaline solutions with nitroethane and nitropropane, compounds which resemble in appearance and in the characteristic color reactions so closely the body obtained from acetoacetic acid as to leave no doubt that the nature of the reaction must be the same in both cases.

[1] Ber. d. chem. Ges., **27**, 155.

[2] The salts have a true azo constitution, as $CH_3C(NO.ONa)(N:N.Ph)$. Bamberger: Ber. d. chem. Ges., **31**, 2626.

[3] The NO_2 group in the azoparaffins can be removed by hydrolysis by means of alkali when heated. Bamberger: *Ibid.*, 2630.

But, as neither nitroethane or nitropropane can, according to Bamberger, give rise to formazyl derivatives—caffezyl compounds in this case—it must be concluded that the dyes from acetoacetic acid also, which resemble so markedly the above nitro compounds, are not caffezyl compounds. It must, however, be remembered that the elementary analysis of the nitro bodies, while pointing to a disazo formula, did not give satisfactory results in the case of carbon and hydrogen. Whether this was due to insufficient purification of the small amount of material at hand, or as in Bamberger's experience,[1] to the marked tendency of these bodies to form oxides of nitrogen during combustion has not yet been determined.

It is hoped that further study of the action of diazocaffeine upon aliphatic compounds will help to clear up the nature of the reaction.

Diazocaffeine Hydrochloride.

After many trials it was found that amidocaffeine can best be diazotized when dissolved in concentrated hydrochloric acid, because the base is only very slightly soluble in dilute acids, and even when in very fine suspension, is only slowly attacked by nitrous acid. Amidocaffeine[2] is dissolved in five times its weight of hydrochloric acid (sp. gr. 1.20) and the solution is well cooled in a freezing-mixture to about —18° C. The calculated quantity of sodium nitrite, dissolved in about four to five times its weight of water, is very slowly run into the bottom of the dish containing the amine, the solution being vigorously stirred by means of a turbine. The temperature is best kept down to —10° C. The foam on the surface of the solution can be broken up by the occasional addition of a few drops of alcohol. The strongly yellow solution, decanted from the solid sodium chloride which separates during the reaction will remain clear for over an hour, if kept in a freezing-mixture. But if the temperature is allowed to rise, a

[1] Ber. d. chem. Ges., **27**, 157.

[2] The amido compound was prepared according to E. Fischer's method [Ann. Chem. (Liebig), **215**, 265]. The heating under pressure was done in autoclaves, by placing in it a large test-tube containing the chlorocaffeine and alcoholic ammonia. Ordinary packing, such as asbestos, rubber, graphite, etc., would not stand. Strips of sheet-lead gave very good satisfaction. In this manner 20 grams of the halogen compound could be used in one operation, and the yield was 17–18 grams of pure amidocaffeine. The temperature of the oil-bath was kept at 150°-160°.

gas, probably nitrogen, is evolved, and a small quantity of very bulky amorphous decomposition-product separates out. The clear solution shows all the reactions of a diazo compound. All the efforts to obtain it in the form of some insoluble salt—as chromate, picrate, or cyanide[1]—proved fruitless. Attempts to reduce it by stannous chloride to a hydrazine were equally unsuccessful. The solution of the diazo salt stains the skin dark-red, quickly changing to brown, which remains permanent for some days.

Apparently the same diazo compound is produced by the action of nitric acid upon amidocaffeine in the cold. This is probably due to a partial reduction of the nitric to nitrous acid.

Caffeine-p-azophenol, $C_8H_9N_4O_2.N:N.C_6H_4(OH)(p)$.—Diazocaffeine couples with phenol in both acid and alkaline solutions, in water or in alcohol. The solution of the diazo salt in hydrochloric acid can at once be added to an ice-cold solution of phenol in water. The azo compound separates immediately as a dark-yellow to an orange mass, resembling in its appearance freshly precipitated ferric hydroxide. The mixture is allowed to stand about an hour, filtered, washed, and dried on a porous plate. The almost black powder is best recrystallized from a large quantity of glacial acetic acid, from which it can be obtained, on slow cooling, in beautiful red needles reflecting light strongly. For analysis it must be recrystallized several times from the same solvent in order to free it entirely from some of the disazophenol, which, as could be judged from the high percentage of nitrogen, was also formed to some extent in the same reaction.

I. 0.1862 gram substance gave 0.3650 gram CO_2, and 0.0778 gram H_2O.

0.1744 gram substance gave 40.4 cc. N at 21°.5 C. and 743.5 mm.

II. 0.1409 gram substance gave 34.7 cc. N at 26° C. and 731.7 mm.

	Calculated for $C_8H_9N_4O_2.N_2.C_6H_4OH$.	Found. I.	II.
C	53.50	53.52	....
H	4.46	4.64	....
N	26.75	26.52	27.26

[1] Ann. Chem. (Liebig), **308**, 64.

The dye is insoluble in cold water and only slightly when heated. It dissolves in dilute alkali hydroxides and carbonates with a deep-red color. Alcohol, even on boiling, takes up only traces of the dye forming yellow solutions. The same is true of chloroform. It is insoluble in ether and benzene. Glacial acetic acid and nitrobenzene are the best solvents for this substance. Concentrated sulphuric acid dissolves the dye with a deep-red color, which instantly changes to an intense violet-blue; this color is changed to a pale-yellow by a drop of potassium dichromate solution, but ferric chloride imparts to it a greenish tint. A slightly alkaline solution of the azo body dyes unmordanted cotton pink, which is discharged by acids, but is brought back by soap solutions.

Caffeine-p-azodimethylaniline, $C_8H_9N_4O_2.N:N.C_6H_4N(CH_3)_2(p)$.—Diazocaffeine combines with dimethylaniline even in the presence of hydrochloric acid. A better yield of the dye is, however, obtained when a solution of the diazo salt in concentrated hydrochloric acid is slowly added to a cold solution of the calculated quantity of dimethylaniline, to which sufficient sodium acetate has been added to take up all the hydrochloric acid. The solution of the dimethylaniline is best cooled by introducing ice directly into it. After standing for from one to two hours the mixture is gently heated on the water-bath until the apparently amorphous precipitate assumes a decidedly crystalline appearance. Ten grams of amidocaffeine gave in this way 9 grams of the azo body. For further purification the dye is recrystallized from boiling chloroform, from which it comes down almost completely on the addition of a very small quantity of ether. The long, dark-red needles, of a beautiful greenish iridescence, were again redissolved in chloroform, and the concentrated solution, while hot, was slowly poured into boiling toluene. The dye is at once precipitated in the form of dark steel-blue needles. A portion of this was then recrystallized from a large quantity of toluene.

I. From toluene: 0.1550 gram substance gave 0.3204 gram CO_2, and 0.0828 gram H_2O.

0.1698 gram substance gave 43.9 cc. N at 25° C. and 745.5 mm.

II. From chloroform and toluene: 0.1865 gram substance gave 0.3885 gram CO_2, and 0.1001 gram H_2O.
0.1916 gram substance gave 49.4 cc. N at 24° C. and 745.5 mm.

III. From chloroform alone: 0.1650 gram substance gave 42 cc. N. at 25° C. and 739 mm.

	Calculated for $C_8H_9N_4O_2.N_2.C_6H_4N(CH_3)_2$.	Found. I.	II.	III.
C	56.30	56.37	56.80	....
H	5.57	5.93	5.96	....
N	28.73	29.18	29.19	28.48

This azo compound can be obtained, as mentioned above, either in cherry-red crystals with a green reflection or in the form of steel-blue needles, or as bluish-red, shining crystals. It is hardly at all soluble in water, dissolves only slightly in dilute, but fairly readily in glacial acetic acid. It is only sparingly soluble in alcohol (red solution), or benzene, not at all in ether. It dissolves in dilute mineral acids forming a deep-red solution. Concentrated sulphuric acid dissolves it with a yellowish-green color, while concentrated hydrochloric acid forms a deep-green solution. The hydrochloride of the base was prepared by dissolving the body in chloroform and passing gaseous hydrochloric acid into the solution. It is a fairly stable salt when dry, but easily decomposed by water.

It dissolves in pure chloroform with a clear red color. But when the chloroform is contaminated with certain impurities then it dissolves the dye with a distinct violet color. Several samples of chloroform on the market responded to this test, giving violet solutions, but on purification gave the red solutions. I was unable to find out just what impurities cause this change in color. Experiments have shown that it is not due to traces of hydrochloric acid, alcohol, or carbonyl chloride.

Reduction with Stannous Chloride.

Two grams of the dimethylaniline dye were dissolved in concentrated hydrochloric acid, and to this solution, while hot, a solution of stannous chloride (10 grams in 20 cc. of

concentrated hydrochloric acid) was added drop by drop until the green color was completely discharged. The solution was then diluted with water to about 300 cc. and the acid partially neutralized. In about an hour the amidocaffeine separated in the form of a white granular powder. It was washed with dilute acid (in which it is almost insoluble), alcohol, and ether. The yield was nearly 1 gram. For analysis it was recrystallized from glacial acetic acid.

0.1643 gram substance gave 50.2 cc. (moist) N at 19°.5 C. and 742 mm.

	Calculated for $C_8H_9N_4O_2NH_2$.	Found.
N	33.50	33.82

The filtrate from amidocaffeine was shaken out with ether, and the residue obtained on evaporating the latter was tested in the usual way for *p*-amidodimethylaniline by means of hydrogen sulphide and ferric chloride. The characteristic methylene blue was thus obtained.

The reaction with stannous chloride is therefore to be represented by the equation:

$$C_8H_9N_4O_2.N:N.C_6H_4N(CH_3)_2 + 4H = C_8H_9N_4O_2NH_2 + NH_2.C_6H_4.N(CH_3)_2.$$

Caffeineazo-2,4-diamidobenzene,

$C_8H_9N_4O_2.N:N.C_6H_3\begin{cases}NH_2\ (o)\\NH_2\ (p)\end{cases}$.—The diazo salt couples very readily with metaphenylenediamine. The reaction was carried out in presence of sodium acetate. The bulky chocolate-brown precipitate becomes almost black on drying. It was recrystallized from glacial acetic acid and analyzed with the following results:

0.1620 gram gave 48.9 cc. N at 26°.5 C. and 736.5 mm.

	Calculated for $C_8H_9N_4O_2.N_2.C_6H_3(NH_2)_2$.	Found.
N	34.15	33.54

It is of a brown color. It is only slightly soluble in the usual organic solvents. Hot glacial acetic acid is the best solvent for it. It does not melt at 285° C. It dissolves in dilute mineral acids with an intense reddish-brown color.

Caffeineazo-β-naphthol, $C_8H_9N_4O_2.N:N.C_{10}H_6OH$. — Five grams of amidocaffeine were diazotized in the usual manner and added to the theoretical amount of β-naphthol in 500 cc. of a 4 per cent solution of potassium hydroxide. The separation of the azo body begins at once, and is greatly hastened and increased by saturating the solution with salt. It was filtered and washed with a solution of salt. On the addition of dilute mineral acid to a warm solution of the alkali salt of the naphthol compound, the free azonaphthol separates in the form of brown flakes mixed with an oil, which on further warming and stirring changes all to a granular precipitate. It was then filtered, washed, first with water then with alcohol and ether, to remove any free β-naphthol, and finally dried on a porous plate. The yield was 6 grams. For analysis the substance was recrystallized from glacial acetic acid; the crystals were collected in two separate crops, the first consisting of minute ponceau-red needles, the second crop being of a somewhat lighter color.

I. 0.2324 gram substance gave 0.5007 gram CO_2, and 0.0976 gram H_2O.

0.2071 gram substance gave 41.4 cc. N at 24° C. and 735.5 mm.

II. 0.1589 gram substance gave 33.9 cc. N at 25°.5 C. and 733 mm.

	Calculated for $C_8H_9N_4O_2.N_2.C_{10}H_6OH$.	Found. I.	II.
C	59.34	48.82	....
H	4.40	4.66	....
N	23.08	22.56	23.63

The dye, insoluble in water, dissolves slowly in a cold solution of sodium carbonate, more rapidly when heated; is soluble in dilute hot alkali hydroxide, forming a deep-red solution. Alcohol dissolves it only slightly, with a violet-blue color; it is insoluble in ether, but dissolves in hot benzene and chloroform with a deep-red color. It dissolves in concentrated sulphuric acid, giving a deep-blue solution, which is intensified by a drop of a solution of ferric chloride, but is discharged by potassium dichromate. This reaction with ferric chloride reminds one in its play of colors of Bülow's reaction for hydra-

zones—a structure sometimes ascribed to oxyazo compounds.

Reaction with Acetoacetic Acid.

Diazocaffeine couples with acetoacetic ester and the free acid, in alkaline solutions, as well as in presence of acetic acid, and even in hydrochloric acid solutions.

After many trials the following method was adopted: 6.5 grams (1 molecule) of the ester are dissolved in about 100 cc. of dilute potassium hydroxide containing 3 grams (1 molecule) of the alkali, and allowed to stand twenty-four hours for complete saponification. 10.5 grams (1 molecule) of amidocaffeine are diazotized in the manner above described, and slowly added to the well-cooled, slightly acidulated solution of the acetoacetic acid, to which about 100 grams of sodium acetate and 300 cc. of water has been previously added. On the first addition of the diazo solution a noticeable evolution of gas takes place, but this soon stops. The azo compound separates at once as a bulky, dark-brown precipitate, which completely fills the beaker. The mixture is allowed to stand in ice about two hours. Salt is then added to saturation, and the solution is gently warmed on the water-bath, whereby the precipitate becomes granular and is easily filtered. On washing, however, with distilled water it swells up again, and can then be filtered only with difficulty. The precipitate, dried on a porous plate, presents a green to blue iridescence, and not infrequently possesses the metallic copper luster of malachite-green. The yield is about 5 grams. It can be recrystallized either from glacial acetic acid or from chloroform. When to the warm solution of the dye in glacial acetic acid a few drops of alcohol or ether are added, it begins to come down at once in the form of a gelatinous, stringy mass, which very soon changes to lumps of dark-blue crystals with a decided green reflection. Alcohol also helps in the crystallization of the substance from chloroform.

I. From glacial acetic acid: 0.2968 gram substance gave 0.4869 gram CO_2, and 0.1214 gram H_2O.

0.1987 gram substance gave 55.5 cc. N at 24° C. and 734.7 mm.

II. From chloroform : 0.2765 gram substance gave 0.4472 gram CO_2, and 0.1105 gram H_2O.

0.1627 gram substance gave 48 cc. (moist) N at 27° C. and 737 mm.

	Calculated for $(C_8H_9N_4O_2N_2)_2C<^{COCH_3}_{CO_2H}$.	Found. I.	Found. II.
C	44.28	44.73	44.15
H	4.06	4.55	4.44
N	31.00	31.12	31.55

The acetoacetic acid compound possesses, as mentioned above, a beautiful dark-green, cantharidine-like luster. It is somewhat soluble in water, dissolving slowly, and forming a reddish-violet solution. On boiling the solution turns deep-blue, of almost the same shade as Fehling's reagent. On cooling the original color comes back. The same changes of color are more marked in dilute solutions of sodium carbonate or hydroxide, in which the dye dissolves, forming intensely colored solutions. It is only slightly soluble in alcohol and benzene, with a pure blue color in the first and a violet-blue in the second. It is fairly soluble in chloroform, and here again the color of the solution is violet-blue. The phenomena of change of color in hot and cold solutions are much more marked in the case of nitroethane and nitropropane compounds. The azo compound shows slight signs of melting at about 200° C., but no further melting is noticeable even at 285° C.

As regards Bülow's reactions, the substance dissolves in concentrated sulphuric acid with a red color, which is not changed either by ferric chloride or potassium dichromate.

Reaction with Propylacetoacetic Acid.

Eight and six-tenths grams (1 molecule) of propylacetoacetic ester mixed with 3 grams (1 molecule) of potassium hydroxide in 100 cc. were allowed to stand twenty-four hours for complete saponification. To this dilution, diluted to about 500 cc. and well cooled, the hydrochloric acid solution of 10.5 grams (1 molecule) of diazotized amidocaffeine was slowly added. Considerable foaming took place at the beginning. The separation of the azo compound greatly in-

creased on the addition of about 100 grams of sodium acetate to the dark-red solution. The mixture, after standing for some time, was saturated with salt and warmed for a short time on the water-bath. The precipitate became granular and was easily filtered. It was washed with a little water and dried on a porous plate. An attempt to remove all the inorganic salts by suspending the well-dried dye in cold water (a treatment successfully employed with other dyes in this work) gave a gelatinous thick mass which proved almost impossible to filter. The yield of the dry substance, well washed with ether, was about 2.8 grams. The substance was dissolved in hot chloroform and to the filtered concentrated solution one-half its volume of ether was added. The crop of crystals which separated in a few hours was recrystallized from glacial acetic acid with the addition of a little alcohol.

0.2493 gram substance gave 0.4217 gram CO_2, and 0.1205 gram H_2O.

0.2054 gram substance gave 55.4 cc. N at 21°.5 C. and 738 mm.

	Calculated for $(C_8H_6N_4O_2N_9)_4C\langle^{C_3H_7}_{COOH}$	Found.
C	46.49	46.17
H	4.80	5.37
N	30.09	30.91

It is a dark-brown crystalline powder with a bluish tint, but lacks the metallic luster of the acetoacetic acid compound. It is very slightly soluble in water, but readily in alkali carbonates and hydroxides—in all cases with a yellow-green color which does not change on boiling. Dilute mineral acids take up small quantities of this azo compound forming a red, cobalt-like solution. The dye is only slightly soluble in benzene, giving a bluish-red solution, while to chloroform, in which it is fairly soluble, it imparts a reddish-violet color. It does not melt at 285° C.

It dissolves in concentrated sulphuric acid, forming a red solution which is not affected by ferric chloride, but is discharged by potassium dichromate.

Reaction with Benzylacetoacetic Acid.

The reaction proceeds as with the propylacetoacetic acid but less smoothly. As this ester is not saponified readily, the alkaline solution, after standing twenty-four hours, was gently warmed for a short time to about 50° C., acidulated and filtered from the unsaponified ester. The coupling was done in presence of sodium acetate. There was considerable foaming on the addition of the diazo salt. There was some flocculent precipitate mixed with a considerable amount of a black oil. It was filtered, thoroughly washed with water, dried on a porous plate, and washed directly on the plate with ether. The dull-black powder was recrystallized twice from chloroform with the addition of ether. The precipitate, at first amorphous, becomes crystalline on standing. The yield of the pure substance was 0.5 gram from 10 grams of amidocaffeine.

0.1802 gram substance gave 0.3320 gram CO_2, and 0.0792 gram H_2O.

0.1872 gram substance gave 49.6 cc. (moist) N at 22° C. and 737 mm.

	Calculated for $(C_8H_9N_4O_2N_2)_2C\begin{matrix}C_7H_7\\CO_2H\end{matrix}$	Found.
C	50.84	50.30
H	4.40	4.88
N	28.47	29.07

This body resembles in its solubility very much the propyl derivative, giving yellow to yellow-green solutions. In Bülow's reaction it is almost identical with the propyl compound. It does not melt at 285° C.

Reaction with Nitroethane.

The diazo salt was added to a well-cooled solution of an excess (1.5 molecule) of nitroethane in about 700 cc. of water containing enough potassium hydroxide to neutralize all the hydrochloric acid of the diazo solution. After standing for some hours the precipitate was filtered off from the dark cherry-red solution, and was well washed with water. The dry substance was dissolved in hot chloroform and the filtered

solution concentrated. The crystals, consisting of deep-blue flakes, were filtered, washed with a mixture of chloroform and ether, and recrystallized once more in the same way. The melting-point remained constant, 218°–219° C. Seven grams of amidocaffeine gave about 0.5 gram of the purified dye. The results of analysis are given below, although the carbon and hydrogen are considerably higher than theory for a disazo body requires. I hope to obtain larger amounts of this body, and establish its composition more exactly.

I. 0.1241 gram substance gave 0.2023 gram CO_2, and 0.0604 gram H_2O.

0.1442 gram substance gave 45.8 cc. N at 22° C. and 739 mm.

II. 0.1224 gram substance gave 38.9 cc. N at 23° C. and 739 mm.

	Calculated for $(C_8H_9N_4O_2N_2)_2C\langle^{CH_3}_{NO_2}$.	Found. I.	II.
C	41.94	44.50	....
H	4.08	5.41	(?)....
N	35.34	35.90	35.80

The nitroethane derivative presents some very peculiar color reactions, similar in nature to those of the acetoacetic acid derivative but more pronounced in character. While insoluble in cold water it dissolves on boiling, giving a deep-blue solution, not unlike that of an ammoniacal copper solution. On cooling, the solution first becomes violet and finally almost entirely red. On reheating, the same phenomena can be observed. This change of color from red to blue and conversely is even more pronounced in dilute alkali solutious, in which the dye is only slightly more soluble than in water. The substance is insoluble in ether, very slightly in benzene (blue solution), readily soluble in chloroform with an intense blue color, and dissolves also in glacial acetic acid, forming a red solution.

Dissolved in concentrated sulphuric acid it gives, like formazyl derivatives,[1] a red solution, which, however, does not change, on standing, into a violet of Bülow's reaction, as

[1] Wedekind: Ber. d. chem. Ges., **30**, 2995.

nitrohydrazones do through intramolecular oxidation;[1] nor does ferric chloride or potassium dichromate bring about this change into the blue or violet.

Reaction with Nitropropane.

The reaction was carried on under the same conditions as with nitroethane. The brown precipitate, after washing and drying, was recrystallized twice from chloroform with the addition of ether and obtained in the form of very light, deep-blue flakes with a slight metallic luster, and melting with decomposition at 237°–238° C. The yield was again small. Ten grams of amidocaffeine furnished about 0.7–0.8 gram of the purified product. The carbon and hydrogen are considerably higher than the theory for a disazopropane requires. What was said under nitroethane applies equally well in this case.

0.2488 gram substance gave 0.4189 gram CO_2, and 0.1186 gram H_2O.

0.1415 gram substance gave 44 cc. N at 21° C. and 739 mm.

	Calculated for $(C_8H_9N_4O_2N_2)_2C\begin{matrix}C_3H_5\\NO_2\end{matrix}$.	Found.
C	43.29	45.95
H	4.35	5.29
N	34.40	35.26

This body is somewhat more soluble in all the solvents than the corresponding nitroethane derivatives. It shows the same peculiar color reactions when its solution in water or dilute alkalies is heated, giving, when hot, a deep-blue solution, which, on cooling, assumes a lavender color.

Towards concentrated sulphuric acid and oxidizing agents it behaves exactly like the nitroethane compound.

CHEMICAL LABORATORY,
UNIVERSITY OF MICHIGAN.
July, 1899.

[1] Bamberger : Ber. d. chem. Ges., **31**, 2631.

THE ACTION OF ETHYL IODIDE ON TARTARIC ESTER AND SODIUM ETHYLATE.

By John E. Bucher.

Introduction.

By the action of the ethylate of sodium or of potassium on symmetrical dibromsuccinic ester (m. p. 58°), a number of investigators have obtained diethoxysuccinic ester. The symmetrical constitution for this compound seems to have been generally accepted. Michael and Bucher,[1] however, showed that it consists mainly of the unsymmetrical diethoxysuccinic ester. They also obtained the same ester by the addition of sodium ethylate to several unsaturated compounds. In no case did they prove the presence of the corresponding symmetrical ester. The following investigation was undertaken with the object of preparing the symmetrical ester and acid so that their properties might be studied.

One of the most obvious methods seemed to be the action of ethyl iodide on disodium tartaric ester. The literature on the subject was not found to be favorable to this method. Meyer and Jacobson,[2] in speaking of the esters of tartaric acid, make the following statement: "Die Wasserstoffatome der alkoholischen Hydroxylgruppen können in diesen Estern durch Natrium und Kalium ersetzt werden; die so entstehenden Alkoholate, wie $C_2H_4(OK)_2(CO_2C_2H_5)_2$, sind zu doppelten Umsetzungen indessen nicht brauchbar." Reference is made to the work of Perkin, Lassar-Cohn, and Mulder. As the original articles, except that of Lassar-Cohn,[3] were not accessible, it was necessary to rely on abstracts in the Chemisches Central-Blatt. In these abstracts no mention is made of the fact that Perkin[4] has studied the action of ethyl iodide and bromide on the above sodium or potassium derivatives. Lassar-Cohn, however, states that Perkin supposed he had probably replaced the sodium in sodium tartaric ester by this

[1] Preliminary articles: Ber. d. chem. Ges., **28**, 2511; **29**, 1792.
[2] Lehrbuch d. organischen Chemie, p. 805.
[3] Ber. d. chem. Ges., **20**, 2003.
[4] Chem. Centrbl., 1867, p. 593.

method. Lassar-Cohn found that no reaction took place on treating the monosodium derivative with methyl iodide or ethyl bromide. The disodium derivative proved to be equally inactive. From these observations he concluded that Perkin probably mistook tartaric ester, regenerated by the action of moisture, for the expected ethoxy derivative. More recently Mulder[1] has published a number of long papers on the action of ethyl chloride on disodium tartaric ester. From the abstracts it appears that he was entirely unsuccessful in preparing diethoxysuccinic ester but that a ketone ester was obtained.

Apparently, the above investigators used the dry sodium or potassium derivatives. It was thought that the reaction might take place in alcoholic solution. A preliminary experiment showed this to be the case, an oil being obtained which was not soluble in alkalies and which gave no color reaction with ferric chloride. After having prepared diethoxysuccinic ester and obtained several salts from it, the abstract of an article by Purdie and Pitkeathly[2] appeared. They had obtained the symmetrical diethoxysuccinic ester by the action of ethyl iodide on tartaric ester and silver oxide. In view of their work, it has seemed desirable to publish the results thus far obtained, although the work is still in progress.

EXPERIMENTAL PART.

One experiment will be described in detail, so that only the variations need be mentioned in the others. To a cooled solution of 27 grams of sodium (25 grams = 2 atoms) in 340 cc. of absolute alcohol 112.5 (2 mols.) grams of tartaric ester and 245 grams of ethyl iodide were added. The solution was boiled with a reflux condenser for twelve hours. The clear solution soon became colored yellow and later red. The red color was not due to the separation of iodine. Carbon dioxide was now passed into the solution, which was very faintly alkaline. The alcohol and excess of ethyl iodide were then distilled off on the water-bath. The residue, after the addition of water, was extracted with ether. This extract was

[1] Chem. Centrbl., **61**, 467; **62**$_2$, 442: **63**, 587; **64**$_2$, 529. 644; **66**, 531; **67**$_1$, 797; **67**$_2$, 345.

[2] *Ibid.*, **70**, 779.

then shaken violently for one-half minute with a solution of caustic alkali to remove any tartaric and ketone esters. The extract was dried with calcium chloride and the ether distilled off on the water-bath. In this way 60 grams of crude product were obtained as a slightly yellowish-red oil.

A part of the aqueous solution, which had been extracted with ether, was acidified and again extracted. So much hydriodic acid was dissolved by the ether that it turned red rapidly from the separation of iodine. This interfered so much that the viscous oil thus obtained was not examined. A solution of calcium chloride was added to the remainder of the aqueous solution. A large quantity of a white precipitate was obtained which was shown to be mainly calcium tartrate (or racemate). The above 60 grams of crude ester were distilled under diminished pressure with a column of beads, using the method described by Michael.[1] About 0.9 of the product came over between 134°–140° at 11.5 mm. The first few cc., being colored by free iodine, were rejected. There was some decomposition at the end of the distillation, about 1 gram of residue remaining in the flask. On redistillation the greater part boiled at 131°.5–136°.5 at 10.5 mm. It was found to contain 53.86 per cent of carbon and 8.10 per cent of hydrogen.

The experiment was repeated many times, varying the conditions and the quantities of the reacting substances. Usually about 2.2 molecules of ethyl iodide were used to each molecule of tartaric ester. In some cases the excess of absolute alcohol was driven from the sodium ethylate by drying *in vacuo* at 230°, and the tartaric ester and ethyl iodide were added to the dry solid. In a few experiments the solution of sodium ethylate was allowed to flow into the boiling mixture of tartaric ester and ethyl iodide. In a few of the earlier experiments the ether extract was not shaken out with caustic alkali, but this was not neglected after finding much tartaric (or racemic) ester in the product, when using one atom of sodium per molecule of tartaric ester. The shaking was not continued more than one-half minute, using a 5 per cent solution of caustic alkali. In one experiment no heat was ap-

[1] J. prakt. Chem., N. F., 46 Nachtrag.

plied, the substances being allowed to stand at the room temperature for two weeks. The quantity of sodium varied from 1 to 2.2 atoms per molecule of tartaric ester. The yield of crude product varied between 50 and 60 per cent of the weight of the tartaric ester used. Evidently other reactions interfere, so that only about one-half of the calculated yield of crude ester is obtained. The products distilled under diminished pressure, with a column of beads, did not have a constant boiling-point, the range being from 4° to 10°. Analyses of the above products showed that, although the yield was fairly constant, the composition varied very much, the percentage of carbon in the various fractions varying from 51.8 to 54.9 per cent.

	Calculated for $C_2H_2(OC_2H_5)_2(CO_2C_2H_5)_2$.	Calculated for $C_2H_2(OH)(OC_2H_5)(CO_2C_2H_5)_2$.	Calculated for $C_2H_2(OH)_2(CO_2C_2H_5)_2$.
C	54.89	50.75	46.60
H	8.40	7.60	6.80

When from 1 to 1.1 atoms of sodium per molecule of tartaric ester were used, the average composition of the fractions was 52.4 per cent of carbon, and when from 2 to 2.2 atoms were used, the average was 54.3 per cent of carbon. As the fractions analyzed did not represent the entire yield, the following additional experiments were made. The entire product was collected in one fraction, only about 5 per cent being lost at each end of the distillation.

Experiment a.—To 5 grams (1 atom) of sodium dissolved in 60 cc. absolute alcohol, 45 grams (1 mol.) of tartaric ester and 130 grams of ethyl iodide were added. After boiling five hours with a reflux condenser the alcohol and excess of ethyl iodide were distilled off on the water-bath. Water was added to the residue and the mixture extracted with ether. The ether extract was shaken out with caustic alkali for one-half minute. The yield of crude product was 23 grams, boiling at 146°–150° at 17 mm. $[\alpha]_D$ was $+31°$ at 20°.

Experiment b.—Proceeded exactly as in Experiment *a*, except that the quantities were as follows: 8 grams (1.07 atoms) of sodium, 100 cc. of absolute alcohol, 67.5 grams (1 mol.) of tartaric ester, 150 grams of ethyl iodide, crude product 36 grams (=53 per cent of the weight of tartaric ester). The

time of boiling was seven hours, and the ester distilled at 145°–150° at 16 mm. $[\alpha]_D$ was +24° at 20°.

Experiment c.—Proceeded as in Experiment *a*, except that the quantities were as follows: 15 grams (3 atoms) of sodium, 180 grams of absolute alcohol, 45 grams (1 mol.) of tartaric ester, and 150 grams of ethyl iodide. The yield of crude product was 20 grams, or 44 per cent of the weight of the tartaric ester. It boiled at 144°–147° at 17 mm. $[\alpha]_D$ was +1.1° at 20°.

Analyses of these three preparations gave the following results:

a,I. 0.2269 gram substance gave 0.4379 gram CO_2, and 0.1637 gram H_2O.

b,I. 0.2042 gram substance gave 0.3954 gram CO_2, and 0.1486 gram H_2O.

b,II. 0.2170 gram substance gave 0.4199 gram CO_2, and 0.1574 gram H_2O.

c,I. 0.2379 gram substance gave 0.4750 gram CO_2, and 0.1788 gram H_2O.

c,II. 0.2056 gram substance gave 0.4085 gram CO_2, and 0.1515 gram H_2O.

	a,I.	*b*,I.	*b*, II.	*c*,I.	*c*,II.
C	52.63	52.81	52.77	54.34	54.19
H	8.02	8.09	8.06	8.36	8.19

From these five analyses and the preceding ones to which reference has already been made, it is evident that when about 1 atom of sodium is used per molecule of tartaric ester the resulting product contains about 52.6 per cent of carbon, and when 2 to 3 atoms of sodium are used the percentage of carbon is increased to about 54.3. These results show that, as might be expected, when only 1 atom of sodium is used, much diethoxysuccinic ester is formed. Also, that when 2 or 3 atoms are used the product consists mainly of this ester. It was possible, in some cases, to obtain a product having the composition of pure diethoxysuccinic ester by fractional distillation under diminished pressure. As these products did not have a constant boiling-point it was evident that fractional distillation did not offer a practical method of obtaining the pure ester or acid.

Accordingly, a specimen of ester having the composition of diethoxysuccinic ester and boiling at 127°.5 to 130° at 9 mm., was saponified by warming with a solution of caustic soda in dilute alcohol. After driving off the alcohol and neutralizing the excess of caustic alkali, a white crystalline precipitate was obtained on the addition of barium chloride.

The results of two analyses of this salt were:

I. 0.5035 gram air-dried salt lost 0.0272 gram at 100°.

II. 0.5762 gram air-dried salt lost 0.0313 gram at 100°, and gave 0.3747 gram $BaSO_4$.

	Calculated for $C_2H_3(OC_2H_5)_2(CO_2)_2Ba.H_2O$.	Found. I.	II.	III.
H_2O	5.01	5.40	5.44	5.11
Ba	38.22	...	38.27	38.44

The results tabulated under III. were obtained from another portion of the same sample of ester. In this case, after saponifying, the solution was acidified and extracted with ether. The acid, which was a very viscous oil, was dissolved in water, neutralized with ammonia, and precipitated with barium chloride.

III. 0.3773 gram air-dried salt lost 0.0193 gram at 100°, and gave 0.2464 gram $BaSO_4$.

The free acid was prepared from the latter specimen of barium salt by adding dilute sulphuric acid and extracting with ether. The ether was removed from the extract at the room temperature, leaving a very viscous colorless oil. The oil was soluble in water and gave no color reaction with ferric chloride solution. On heating a drop of the oil on a watch-glass over the water-bath, bubbles were given off and it turned into a white solid. The white solid was very soluble in water, and gave an intense red color with ferric chloride solution. It was oxalacetic acid. This reaction and the composition of the barium salt led to the conclusion that the oil was not the symmetrical compound, but that it was identical with the unsymmetrical diethoxysuccinic acid studied by Michael and Bucher. This was confirmed by dissolving the oil in water, neutralizing with ammonia, and making the salts of silver, calcium, and lead by precipitation.

The silver salt, which was a white crystalline precipitate,

was dried in the air to constant weight and analyzed with the following result:

0.6499 gram salt gave 0.4428 gram AgCl.

	Calculated for $C_2H_2(OC_2H_5)_2(CO_2Ag)_2$.	Found.
Ag	51.40	51.29

The calcium salt separated as a white crystalline precipitate. These microscopic crystals were six-sided plates, many having four sides curved, so that they had the same appearance as sections cut from a barrel parallel to its axis. The salt also showed great creeping power when freshly precipitated. These properties are very characteristic of the calcium salt of unsymmetrical diethoxysuccinic acid. An analysis of the air-dried calcium salt gave the following result:

0.4963 gram salt gave 0.2553 gram $CaSO_4$.

	Calculated for $CH_2(OC_2H_5)_2(CO_2)_2Ca.H_2O$.	Found.
Ca	15.28	15.14

The lead salt also was a white crystalline precipitate. The analysis of the air-dried salt gave the following result:

I. 0.5018 gram salt gave 0.3553 gram $PbSO_4$.

II. 0.5262 gram salt gave 0.3729 gram $PbSO_4$.

	Calculated for $C_2H_2(OC_2H_5)_2(CO_2)_2Pb.H_2O$.	Found. I.	Found. II.
Pb	48.23	48.35	48.40

The properties of the free acid and the composition of these four salts leave no doubt that the acid has the constitution

$$\begin{array}{l} C(OC_2H_5)_2CO_2H \\ | \\ CH_2CO_2H \end{array}.$$

This complicated the matter somewhat, and in order to obtain a large quantity of ester all the remaining specimens of the older preparations were united. The 90 grams thus obtained were subjected to fractional distillation. The main lot boiled at 138°–143° at 13 mm., about 16 cc. being rejected at the beginning and 6 cc. at the end of the distillation. This fraction was again distilled at 133°–137° at 11 mm., about 3 cc. being rejected at each end. This was redistilled, and the first two-thirds, boiling at 133°–135°.5 at 11 mm., was collected

as fraction *k*. $[\alpha]_D$ at 23° was +1°.4 for this fraction. All the other fractions were reunited and found to boil at 133°–139° at 11 mm. This will be called fraction *n*. $[\alpha]_D$ at 23° was +2°.5 for this fraction.

The average of three analyses of fraction *k* and four of fraction *n* gave the following result :

	Calculated for $C_2H_3(OC_2H_3)_3(CO_2C_2H_5)_2$.	Found. *k*	Found. *n*
C	54.89	54.72	53.92
H	8.40	8.22	8.07

Fraction *k* had the composition of a nearly pure diethoxysuccinic ester. Exactly 5 grams were saponified by caustic soda dissolved in dilute alcohol. After the alcohol had been driven off on the water-bath the excess of alkali was neutralized and an aqueous solution of 5.5 grams of calcium chloride added. The volume of the solution was 150 cc., and, after filtering, the precipitate was washed with 150 cc. of water. The yield of air-dried salt was 2.51 grams, but on concentrating the filtrate and washings an additional 0.2 gram was obtained. This total of 2.71 grams of calcium salt corresponds to 54 per cent of unsymmetrical ester in fraction *k*. The salt was not quite pure, however, as it contained 15.98 per cent of calcium. Probably 45 per cent of the unsymmetrical ester is near the truth. This calcium salt, combined with that obtained by saponifying the remainder of fraction *k*, was acidified with dilute acid and extracted with ether. The colorless viscous oil thus obtained yielded the pure calcium salt, an analysis giving 15.33 per cent of calcium.

Fraction *n* was treated exactly as fraction *k* had been. From 5 grams of ester 1.77 grams of air-dried calcium salt, corresponding to 35 per cent of unsymmetrical ester, were obtained. This calcium salt seemed not to be quite as pure as that from fraction *k*, and probably 25 per cent is about the quantity of unsymmetrical ester present. The remainder of fraction *n* was saponified and treated with calcium chloride as before. After filtering off the insoluble calcium salts the filtrate was acidified and extracted with ether. On evaporation, a very viscous colorless oil was obtained, which did not give any color with ferric chloride solution, before or after it had

been heated to 100°. It did not solidify on standing over sulphuric acid in the ice-chest for a week. After neutralizing, it did not give a precipitate with barium, calcium, or lead salts. Both the neutral and acid potassium salts are very soluble in water. $[\alpha]_D$ for this crude acid in aqueous solution at 18° was +2°. The oil was neutralized with caustic potash and the solution evaporated to a doughy mass on the water-bath. Absolute alcohol was then added slowly. In this way it was possible to separate out a nice crystalline precipitate. This salt, dried at 150°, gave the following result on analysis:

I. 0.3244 gram salt gave 0.2010 gram K_2SO_4.

Another specimen was prepared in the same way, dried at 150°, and analyzed with the following result:

II. 0.4172 gram salt gave 0.2573 gram K_2SO_4.

	Calculated for $C_3H_5(OC_2H_5)_2(CO_2K)_2$.	Found. I.	II.
K	27.71	27.81	27.68

An aqueous solution of this salt had no action on polarized light. The pure acid was prepared from this potassium salt by acidifying and extracting with ether. On evaporating the ether *in vacuo* the acid separated as an oil, which quickly solidified at the temperature of the room. Without further purification it was dried over sulphuric acid in a partial vacuum for a week. It melted at 97°–99°. The results of an analysis were as follows:

0.2273 gram substance gave 0.3890 gram CO_2, and 0.1416 gram H_2O.

	Calculated for $C_3H_5(OC_2H_5)_2(CO_2H)_2$.	Found.
C	46.67	46.58
H	6.92	6.87

The aqueous solution of the acid had no effect on polarized light. When neutralized with ammonia, it did not give precipitates with solutions of lead, calcium, or barium salts of the ordinary strength. It was not changed on heating to 100°. A portion was boiled with 10 per cent sulphuric acid with reflux condenser, and on adding a solution of phenylhydrazin sulphate, no precipitate was formed. This shows

that no pyruvic acid was formed. These two experiments show how the above acid differs from the unsymmetrical one, and it evidently has the constitution represented by the formula

$$\begin{array}{l} CH(OC_2H_5)CO_2H \\ | \\ CH(OC_2H_5)CO_2H \end{array}.$$

The remainder of this acid was boiled with water and barium carbonate. The solution was filtered and evaporated on the water-bath. The salt which crystallized out was air-dried, and, on analysis, gave the following result:

0.5025 gram salt lost on heating one hour and a half, finally at 190°–215°, 0.0872 gram, and gave 0.2836 gram $BaSO_4$.

	Calculated for $C_2H_2(OC_2H_5)_2(CO_2)_2Ba.4H_2O$.	Found.
Ba	33.23	33.22
H_2O	17.48	17.35

This salt was soluble in about 12 parts of water at the room temperature and had no effect on polarized light. Nothing else was separated in the pure form from these 90 grams of ester, although there must have been a number of other compounds present. It was at this point that the preparations already referred to as *a*, *b*, and *c* were made.

Fifteen grams of preparation *b* were saponified with caustic soda in dilute alcoholic solution. After driving off the alcohol on the water-bath, and neutralizing the excess of alkali, calcium chloride solution was added. Only 50 milligrams of precipitate were obtained, and this was not the calcium salt of unsymmetrical diethoxysuccinic acid. Hence, very little, if any, of the unsymmetrical ester is formed when 1 atom of sodium is used per molecule of tartaric ester. This result is confirmed below under the saponification of fraction *a*. The filtrate from the above calcium salt was acidified with sulphuric acid and extracted ten times with ether. The first four of these extracts were united and yielded 5.4 grams of a very viscous oil, and the remaining six yielded 2.6 grams more. Neither specimen gave, before or after heating to 100°, a color reaction with ferric chloride, nor did they solidify in the ice-chest.

The specimen weighing 5.4 grams was converted into the barium salt by means of barium carbonate. The solution was filtered and evaporated to 14 cc. The salt which crystallized out on cooling was air-dried. The following results were obtained on analysis:

I. 0.4767 gram salt lost, on heating to 110°–130° for one hour, 0.0840 gram, and gave 0.2694 gram $BaSO_4$.

II. 0.4026 gram salt lost, on heating to 155° for one hour, 0.0725 gram, and gave 0.2277 gram $BaSO_4$.

	Calculated for $C_2H_2(OC_2H_5)_2(CO_2)_2Ba.4H_2O$.	Found. I.	II.
Ba	33.23	33.26	33.29
H_2O	17.48	17.62	18.01

$[\alpha]_D$ for this sample in aqueous solution was +14°. The salt was recrystallized from water by evaporating *in vacuo* over sulphuric acid. The crystals which first separated were short and compact, looking exactly like those which were prepared by Purdie and Pitkeathly's method for comparison. Later, however, the substance crystallizing out had a different appearance. $[\alpha]_D$ for the recrystallized salt was now +18°. This is lower than the value given by Purdie and Pitkeathly, showing the difficulty in separating the active from the inactive salt. There is no doubt that the part first separating out is the barium salt of *d*-diethoxysuccinic acid. The salts, which remained in the mother-liquor from the first crystallization of the barium salt, were much more soluble and less active than the latter. The efforts to isolate them were entirely unsuccessful.

The 2.6 grams of acid from the last six extractions were dissolved in a very small quantity of water, and a concentrated solution of lead acetate added. The white precipitate thus prepared was dried at 100° and gave the following result on analysis:

0.4828 gram salt gave 0.3823 gram $PbSO_4$.

	Calculated for $C_2H_2OH(OC_2H_5)(CO_2)_2Pb$.	Found.
Pb	54.03	54.07

The salt does not separate out unless the solution is rather concentrated, and it was not examined in polarized light.

The existence of the hydroxyethoxysuccinic ester and acid was confirmed by the next experiment.

Preparation *a* was saponified in the same manner as the above. As in the former case, there was little or no precipitate of insoluble calcium salt, proving the absence of the unsymmetrical ester. The acid was converted into the barium salt in the usual manner. The solution was then evaporated on the water-bath until a scum began to form. Absolute alcohol was added to the hot mass and the pasty precipitate rejected. The filtrate was treated in the same manner. This last filtrate was concentrated, acidified, and extracted with ether. The acid thus obtained was added to a strong solution of lead acetate, and the white precipitate thus obtained, after being dried to a constant weight in the air-bath, contained 53.9 per cent of lead. This corresponds to the percentage of lead in the lead salt of hydroxyethoxysuccinic acid.

Preparation *c* (from 3 atoms of sodium per molecule of tartaric ester) was lost, but not before it was shown to contain much unsymmetrical diethoxysuccinic ester. One gram was saponified in the usual manner. From this an insoluble calcium salt separated in abundance. The acid prepared from this showed the characteristic conduct of the unsymmetrical acid on heating to 100°, and toward ferric chloride solution before and after heating.

It is evident from the fact that the unsymmetrical diethoxy ester was formed from tartaric ester, a compound having the symmetrical constitution, that the reaction must be more complicated than the simple replacement of hydrogen by ethyl. The following preliminary experiment may throw some light on the subject: When 1 molecule of tartaric ester is boiled with 2 atoms of sodium, dissolved in absolute alcohol, a yellowish-brown salt begins to separate in about fifteen minutes, and the reaction seems to be complete within an hour. The salt can be filtered off, and on evaporating the filtrate there seems to be nothing left except a small quantity of the same substance.

The salt can be acidified and extracted with ether. The very viscous oil is apparently a ketone ester, as it gives a deep-red color with ferric chloride and reacts with

phenylhydrazine. On neutralizing the aqueous solution which had been extracted with ether, and adding calcium chloride solution, a small quantity of a white precipitate was obtained. It was the calcium salt of tartaric acid or its isomers.

The yellowish-brown salt, when boiled with caustic soda and evaporated to a small bulk, yields sodium oxalate very abundantly. Also, when it is dissolved in dilute sulphuric acid, and a solution of phenylhydrazine sulphate added, a large quantity of oily product is formed immediately. This turns to a sticky solid mass in the ice-chest. When this substance is boiled with caustic alkali it passes into solution. From this highly colored solution acids precipitate a substance which it is difficult to obtain pure. By alternately boiling with bone-black and crystallizing from dilute alcohol it was obtained nearly colorless. With ferric chloride it gave the violet color-test for 1-phenyl-5-pyrazolon-3-carboxylic acid. The melting-point also corresponded to that of this compound, but the crystals had a different appearance from those prepared by other methods. The percentage of carbon was about 0.5 higher than the calculated amount. It was probably impure 1-phenyl-5-pyrazolon-3-carboxylic acid, but this conclusion can only be regarded as tentative. If oxalacetic ester is formed, this might possibly form an ethoxy ester by the action of ethyl iodide on its sodium salt, and this, by the addition of sodium ethylate, form an unsymmetrical product. W. Wislicenus got a carbon homologue from the sodium salt of oxalacetic acid, but he did not follow the reaction very far.

One experiment has been made, using ethyl bromide instead of ethyl iodide with the sodium ethylate and tartaric ester. The yield of ester was fully as good as with ethyl iodide, and it has the great advantage of not forming halogen by-products.

RHODE ISLAND AGRICULTURAL COLLEGE,
KINGSTON, R. I.

NOTE.

Improvements in the Manufacture of Sulphuric Acid.

In a recent number of the Journal of the Society of Chemical Industry, there is an interesting address by Professor G. Lunge from which the following is taken :

"We naturally begin with *sulphuric acid*, and here we are at once confronted with the greatest revolution which has taken place since that acid became a commercial product in the days of Ward and Roebuck; a revolution beside which the invention of the Gay-Lussac and Glover tower, let alone that of plate-columns and the like, sinks into insignificance. I mean, of course, the total abolition of the vitriol chamber, and even of the use of nitrous fumes as oxygen carriers, by the use of the catalytic power of platinum, perhaps also by that of ferric oxide and other substances, a reaction of which the first literary landmark is the British patent of Phillips taken out in 1831, but which has been mainly worked out by German chemists, Döbereiner, Magnus, Wöhler, Plattner, Clemens Winkler, and others, not to forget my originally German countryman, Messel. All of these had been content to apply that reaction to the preparation of sulphur trioxide, in the shape of Nordhausen fuming acid. Some years ago it was whispered that the Badische Anilin and Soda Fabrik had perfected and cheapened that process to such a degree that they were manufacturing ordinary sulphuric acid in this way cheaper than by the old process, and that they were gradually pulling down their vitriol chambers. This was hardly believed to be possible, and was taken as an exaggeration of the truth. But last year the Badische applied for patents in all countries, some of which are now published. Other firms have proceeded on the same lines partly with other contact substances, among them oxide of iron in the shape of pyrites cinders, with which I myself experimented many years ago as a means for combining SO_2 with oxygen."

"We now know the Badische invention. The principal feature of it is their discovery that it is necessary to get rid of the heat of the reaction in order to obtain a quantitative union of sulphur dioxide and oxygen to sulphur trioxide, and that under such circumstances a *complete* union is obtained, even when using ordinary dilute technical gases, such as result from pyrites burners. As a measure of the progress made, I may remind you that, as I wrote at the end of the year 1897 in 'The Mineral Industry of the United States and Other Countries,' p. 130 :—

"'Probably 67 per cent must be considered very good work, and the remaining 33 per cent. of sulphurous acid must be sent into lead chambers, together with better gas from other burners.'

"In lieu of 67 per cent. we must *now* speak of 98 per cent.

"The said removal of the heat of reaction can be effected in such a way as to heat the entering gases to the temperature necessary for the reaction, so that the contact stoves when once started work automatically.

"A further important feature of the Badische invention consists in the discovery of the reason why the contact-substance (platinized asbestos) as hitherto used, in a short time wholly or partly loses its activity, and of means for preventing this. The cause of this loss of activity has been traced to certain constituents in the technical gases, the deleterious action of which was hitherto unknown. To remove these, a special washing process has been invented, which, in a certain direction, goes far beyond any attempt at purification published up to this time.

"Of course there is still a wide step from knowing those principles, to carrying them out as paying concerns; although former employees have offered their knowledge of the principles referred to for sale for several years, it is not known that anyone has successfully manufactured from their information. But it is absolutely certain that at Ludwigshafen itself that step has been made, and that in more than one large works the lead chambers are either entirely abolished or at least moribund.

"This is a sad outlook for those whose capital is, to a great extent, sunk in the old vitriol process! But as yet very many of them need not despair. It would appear that in the case of less concentrated acids, up to the point of chamber acid, or even Glover tower acid, the chamber process can still compete with the catalytic process, and for acid of such strength there would be no need whatever to incur the expense of introducing the catalytic system. Indeed the Badische patents state:—

"'Acids weaker than up to 50° Bé. (that is, containing about 63 per cent H_2SO_4) can, according to this invention, be prepared at least as cheaply as by means of the chamber process, and all stronger acids are produced by this invention more cheaply, the advantages being greater the stronger the acid.'

"In cases, however, where the purity of the acid is an important point, the Badische process is advantageous even for dilute acids, for all the acids made by this process are exceptionally pure and especially free from arsenic. It is worth

mentioning also that the cost of plant for the new process is considerably less than that of the old one and requires less space. Thus, in the Badische works, I am told that the capital outlay for a plant which is used for making all grades of acid from anhydride down to weak acid costs about two-thirds as much as a plant calculated to yield a corresponding quantity of concentrated oil of vitriol of 66° Bé.

"Since in the case of less concentrated acids, say up to about 80 per cent. H_2SO_4, the chamber process can still compete for cheapness with the catalytic process, the enormous capital sunk in vitriol chambers for the manufacture of superphosphates, of salt-cake and all analogous cases would still remain operative; but certainly vitriol makers are now put upon their mettle to look out for the best means for improving the efficiency of their plant and of their method of working. For various reasons I shall abstain from going into reasons on that point; but I may be excused for indulging in some "music of the future," in mentioning the advantages to be derived from using oxygen in a more concentrated form than that of atmospheric air. The proposal of Messel for employing electrolytic oxygen, or that of myself for Brin's oxygen, came undoubtedly too early even for the manufacture of SO_3 at its former prices, but since we can make a gaseous mixture rich in oxygen, very cheaply by liquefying air, the possibility of employing that mixture in the manufacture of sulphuric acid is decidedly less removed from the sphere of actuality. In Germany 'Linde-Luft,' as it is there called, is already an article of commerce; it is actually used for the preparation of an explosive, and it is at least thought of even for such uses as the working of gas-producers. In America they are going ahead with it much faster, if we may credit even a portion of the sensational accounts which reach us. Do not let us forget that in this case the advantage will again lie with those nations who possess cheap force in the shape of water-power, in order to produce liquid air.

"Coming back from the aërial regions to the solid ground of present facts, there seems to be no doubt that the catalytic processes have a decided advantage over the chamber process where acid of a higher concentration than Glover acid or of special purity is required.

"Proof of this is the fact that one after the other the great German colour works, where mainly strong acid is used, have introduced the new processes, or are making preparations for doing so. But even here some comfort remains to the owners of lead chambers, and glass or platinum retorts and the like. Where the initial cost of plant has been written off to a great

extent during former better years, and especially in small-sized works they will, in the face of the cost of new plant and of the royalties to be paid for the processes, be able to hold on to their existing plant for a number of years. The first to change will be probably those works where much waste acid is to be disposed of and reconcentrated, as for instance in the manufacture of explosives. But I must content myself with these general allusions."

REVIEWS.

THE SOLUBLE FERMENTS AND FERMENTATION. By J. REYNOLDS GREEN, Sc.D., F.R.S., Trinity College, Cambridge; Professor of Botany to the Pharmaceutical Society of Great Britain; Formerly Senior Demonstrator in Physiology in the University of Cambridge. Cambridge University Press. 1899. 480 pp.

This book, which is one of the Cambridge Natural Science Manuals, Biological Series, aims to give a full and concise account of the present state of our knowledge concerning the so-called soluble ferments. The subject is treated historically so that we have, in addition, a more or less complete account of the lines along which development has taken place up to the present time. This gives the volume added value as a book of reference, a value which is increased by the very full bibliography at the end of the volume.

The first chapter deals with the nature of fermentation and its relation to enzymes, followed by a classification of enzymes, in which the latter are grouped according to the materials on which they work. While the list is not wholly complete, mention is made of *urease* which forms ammonium carbonate from urea, and the new *zymase* of Buchner, *i.e.*, the alcohol-producing enzyme. Four chapters are devoted to a discussion of vegetable and animal diastase, while inulase, cytase and other cellulose-dissolving enzymes, urease, pectase, oxidases or oxidizing enzymes, are each given a chapter descriptive of their chemico-physiological properties. To proteolytic enzymes and proteolysis three chapters are devoted. The clotting enzymes are likewise given due consideration, while fat-splitting enzymes and sugar-splitting enzymes are duly considered, as are also alcoholic fermentation, the fermentative power of protoplasm, the secretion of enzymes, the constitution of enzymes, while a brief account of the theories of fermentation closes the volume.

We have in this book by Dr. Green, a very readable statement of existing knowledge regarding enzymes, but we fail to find in it much that is original. This, perhaps, is hardly

to be expected, since the book aims primarily, as stated in the preface, "to put together as far as possible, the results reached up to the present time." The book is especially opportune at the present moment, since we have now reached a point in our knowledge where we are practically compelled to drop the old distinction between organized and unorganized ferments, and the more thoroughly knowledge is disseminated regarding the part which enzymes play in intracellular, metabolism, so much the sooner will the chemical and physiological world acquire a true appreciation of the many points of similarity between the metabolic processes of higher and lower organisms. Enzymes are unquestionably intimately associated with the living substance of protoplasm, and consequently we may look for an intimate relationship between fermentation and the ordinary processes of metabolism. For furthering the spread of knowledge regarding these points, the present volume is especially well adapted, and the book is to be welcomed as a valuable addition to the store-house of knowledge.

Careful scrutiny of the subject-matter composing some of the chapters of the book must lead to criticism of the thoroughness with which the work of compilation and selection has been done. Thus, on pages 264–267, dealing with the myosin ferment and the proteids of muscle, we look in vain for any reference to the very important work of Von Furth on this subject, which appeared in volumes 36 and 37 of the *Archiv für experimentelle Pathologie und Pharmakologie*, 1895–1896. Further, in chapter XVI, dealing with thrombase, the fibrin-ferment, we find among the various facts and theories of blood-coagulation discussed, no mention of the widely quoted work of Lilienfeld on this subject, which appeared in 1894, and which is now incorporated in all recent text-books of physiological chemistry. Again, on page 188, where the characteristic products of trypsin-proteolysis are discussed, we look in vain for any mention of the very important work of Kossel and his coworkers on the hexone bases, arginin, lysin, and histidin, which are now recognized as among the characteristic end-products of trypsin-proteolysis. Among these bases, lysin was first emphasized as a product of trypsin-proteolysis in 1891 by Drechsel and Hedin. These are a type of criticisms, however, which apply to nearly all books. Perfection is not of this world. It may be, however, that these omissions simply represent the author's opinion of the relative value of the omitted facts as contrasted with those presented. If this is the case, the reviewer cannot agree with the author in his estimate of their relative value in any discussion of soluble ferments and fermentation.

R. H. CHITTENDEN.

EINFÜHRUNG IN DIE CHEMIE IN LEICHTFASSLICHER FORM. VON PROF. DR. LASSAR-COHN. Königsberg, Hamburg und Leipzig; Verlag von Leopold Voss.

In this volume Prof. Lassar-Cohn offers a text-book of chemistry for university-extension work. He acknowledges in his preface that the problem of how to write a book for this purpose is difficult, and that the task first seemed to him impossible. The present volume is a natural sequence of his popular lectures published under the title "Die Chemie im täglichen Leben,"[1] and every reader of those admirable lectures will feel that Lassar-Cohn was well qualified to attempt a text-book simpler in form and matter than those used in colleges, yet addressed to thinking men and women.

The descriptive part of the book treats of the more important elements and inorganic compounds, omitting all reference to less important substances; the theoretical part covers the same field as an ordinary text-book of inorganic chemistry. In the chapter on carbon, the commonest organic compounds and their relations to the simpler hydrocarbons are briefly discussed, while the fundamental theories of organic chemistry including substitution, valence, Kekulé's benzene theory, isomerism, ortho, meta, and para compounds, are explained clearly and simply.

The impression left on the reviewer is that the author has succeeded in his task; that he has written a book simple enough to enable an intelligent working man to master it with the help of experimental lectures, and scientific enough to give the learner a solid basis for further work, should opportunity offer. The book should interest us all in view of the spread of the university-extension movement in this country.

E. R.

[1] The English translation of this book by M. M. Pattison Muir, "Chemistry in Daily Life" was reviewed in This JOURNAL, 19, page 81.